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(54) Title: LUTZOMYIA LONGIPALPIS POLYPEPTIDES AND METHODS OF USE

(57) Abstract: Substantially purified salivary lu. longipalpis polypeptides, and polynucleotides encoding these polypepetides are disclosed. Vectors and host cells including the lu. longipalpis polynucleotides are also disclosed. In one embodiment, a method is disclosed for inducing an immune response to sand fly saliva. In other embodiments, methods for treating, diagnosing, or preventing leishmaniasis are disclosed.

LUTZOMYIA LONGIPALPIS POLYPEPTIDES AND METHODS OF USE

PRIORITY CLAIM

This application claims the benefit of U.S. Provisional Application No. 60/422,303, filed October 29, 2002, which is incorporated herein by reference.

FIELD

The disclosure relates to proteins substantially purified from Lutzomyia longipalpis (*Lu. longipalpis*) sand fly salivary glands, or recombinant vectors expressing these proteins, and to an immune response produced to these proteins. This disclosure also relates to the production of an immune response that affects survival of Leishmania.

BACKGROUND

Leishmaniasis is a group of diseases caused by protozoa of the genus *Leishmania* and affect many millions of people worldwide. In humans, infection with the parasite manifests either as a cutaneous disease caused mainly by *L. major, L. tropica*, and *L. mexicana*; as a mucocutaneous disease caused mainly by *L. brasiliensis*; or as a visceral disease caused mainly by *L. donovani* and *L. chagasi*. In canids, Leishmania infections manifest as a visceral disease that can result in high death rates.

All leishmanial diseases are transmitted to their vertebrate hosts by phlebotomine sand flies, which acquire the pathogen by feeding on infected hosts and transmit them by regurgitating the parasite at the site of a subsequent blood meal (Killick-Kendrick, Biology of *Leishmania* in phlebotomine sand flies. In Biology of the Kinetoplastida. W. Lumsden and D. Evans, editors. Academic Press, New York. 395, 1979).

While obtaining a blood meal, sand flies salivate into the host's skin. This saliva contains anticlotting, antiplatelet, and vasodilatory compounds that increase the hemorrhagic pool where sand flies feed (Ribeiro *et al., Comp. Biochem. Physiol.* 4:683, 1986; Charlab *et al., Proc. Natl. Acad. Sci. USA.* 26:15155, 1999). Some of these components are additionally immunomodulatory. For example, the New World sand fly *Lutzomyia longipalpis* contains the 6.5 kDa peptide, maxadilan, which is the most potent vasodilator known (Lerner *et al., J. Biol. Chem.* 17:11234, 1991). Maxadilan additionally has immunosuppressive activities of its own (Qureshi *et al., Am. J. Trop. Med. Hyg.* 6:665, 1996), as do many persistent vasodilators such as prostaglandin E_2 (Makoul *et al., J. Immunol.* 134:2645, 1985; Santoli and Zurier, *J. Immunol.* 143:1303, 1989; Stockman and Mumford, *Exp. Hematol.* 2:65, 1974) and calcitonin gene-related peptide (Nong *et al., J. Immunol.* 1:45, 1989). Old World sand flies do not have maxadilan but instead use AMP and adenosine as vasodilators (Ribeiro *et al., J. Exp. Biol.* 11:1551, 1999). Adenosine is also an immunomodulatory component, promoting the production of IL-10 and suppressing TNF-α and IL-12 in mice (Hasko *et al., J. Immunol.* 10:4634, 1996; Webster, *Asian Pac. J. Allergy Immunol.* 2:311, 1984; Hasko *et al.,*

FASEB J. 14:2065, 2000). Despite what is known about the role of sand fly saliva and disease transmission, much remains unknown, and an effective vaccine does not exist. Thus, there is a need for agents that can be used to induce an immune response to the organisms that cause leishmaniasis.

SUMMARY

The present disclosure relates to salivary proteins from sand fly vectors of *Lutzomyia longipalpis* (*Lu. longipalpis*) and the nucleic acids that encode these proteins. Methods of producing an immune response in a subject are also disclosed.

Substantially purified salivary *Lu. longipalpis* polypeptides are disclosed herein. Also disclosed are polynucleotides encoding the *Lu. longipalpis* polypeptides.

Methods are disclosed for inducing an immune response using a therapeutically effective amount of a substantially purified salivary *Lu. longipalpis* polypeptide as disclosed herein, or the polynucleotide encoding a *Lu. longipalpis* polypeptides disclosed herein.

In another embodiment methods are disclosed herein for inhibiting the symptoms of a *Leishmania* infection or for preventing a *Leishmania* infection in a subject. The methods include administering to the subject a therapeutically effective amount of a *Lu. longipalpis* polypeptide, or a polynucleotide encoding a *Lu. longipalpis* polypeptide. In two non-limiting examples, more than one *Lu. longipalpis* polypeptide can be administered, or at least one *Lu. longipalpis* polypeptide in conjunction with a *P. ariasi* or *P. perniciosus* polypeptide.

Also disclosed herein are methods of diagnosing *Leishmania* infection in a subject. The methods include contacting a solid substrate comprising at least three, six, or ten *Lu. longipalpis* polypeptides, or an immunogenic fragment thereof, contacting the solid substrate with a sample obtained from the subject and detecting binding of a component of the sample to at least one polypeptide on the solid substrate. Detection of binding of the component to the substrate indicates that the subject is infected with *Leishmania*.

Pharmaceutical compositions are disclosed including a pharmaceutically acceptable carrier and a *Lu. longipalpis* polypeptide.

The foregoing and other features and advantages will become more apparent from the following detailed description of several embodiments, which proceeds with reference to the accompanying figures.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 is a set of bar graphs showing the levels of antibodies against *Lutzomyia longipalpis* (*Lu. longipalpis*) saliva in sera of individuals. Human sera were obtained at time 0 (negative anti-*Leishmania* serology (S^-) or negative DTH (DTH^-)) and 6 months later (positive anti-*Leishmania* serology (S^+) or positive anti-*Leishmania* DTH (DTH^+)). ELISA was performed with these sera using salivary gland sonicate of the sand fly *Lu. longipalpis*. FIG. 1A is a bar graph of anti-saliva IgG levels in individuals who converted from $S^- \rightarrow S^+$ and those who converted from DTH^- to DTH^+. FIG. 1B is a bar graph of anti-saliva IgE levels in the individuals described in FIG. 1A. FIG. 1C is a

bar graph of anti-saliva IgG1 levels in the individuals described in FIG. 1A. FIG. 1D is a bar graph of anti-saliva IgG4 levels in the individuals described in FIG. 1A. The non-parametric paired Wilcoxon test was used to compare levels of anti-*Lu. longipalpis* saliva antibodies at time 0 and after 6 months. *P* value < 0.05 was established as the significance level.

FIG. 2 is a set of two digital images and a bar graph showing salivary proteins recognized by Western blot analysis. FIGS. 2A and 2B are digital images of a Western blot of *Lu. longipalpis* salivary proteins reacted to human sera of individuals who converted from $S^- \rightarrow S^+$ to *Leishmania* (lanes 1–6) or from $DTH^- \rightarrow DTH^+$ to *Leishmania* (lanes 7–14). Symbols: –, time 0; +, 6 months. FIG. 2C is a bar graph of the frequency of salivary proteins recognized by sera of 13 individuals who converted from $DTH^- \rightarrow DTH^+$ to *Leishmania*. The x-axis shows the different *Lu. longipalpis* salivary proteins (labeled by the approximate molecular weight) recognized by Western blot analysis, while the y-axis indicates the number of human sera recognizing a particular salivary protein.

SEQUENCE LISTING

The nucleic and amino acid sequences listed in the accompanying sequence listing are shown using standard letter abbreviations for nucleotide bases, and three letter code for amino acids, as defined in 37 C.F.R. 1.822. Only one strand of each nucleic acid sequence is shown, but the complementary strand is understood as included by any reference to the displayed strand. In the accompanying sequence listing:

SEQ ID NO: 1 is the amino acid sequence of LJL34.
SEQ ID NO: 2 is the nucleic acid sequence of LJL34.
SEQ ID NO: 3 is the amino acid sequence of LJL18.
SEQ ID NO: 4 is the nucleic acid sequence of LJL18.
SEQ ID NO: 5 is the amino acid sequence of LJS193.
SEQ ID NO: 6 is the nucleic acid sequence of LJS193.
SEQ ID NO: 7 is the amino acid sequence of LJS201.
SEQ ID NO: 8 is the nucleic acid sequence of LJS201.
SEQ ID NO: 9 is the amino acid sequence of LJL13.
SEQ ID NO: 10 is the nucleic acid sequence of LJL13.
SEQ ID NO: 11 is the amino acid sequence of LJL23.
SEQ ID NO: 12 is the nucleic acid sequence of LJL23.
SEQ ID NO: 13 is the amino acid sequence of LJM10.
SEQ ID NO: 14 is the nucleic acid sequence of LJM10.
SEQ ID NO: 15 is the amino acid sequence of LJL143.
SEQ ID NO: 16 is the nucleic acid sequence of LJL143.
SEQ ID NO: 17 is the amino acid sequence of LJS142.
SEQ ID NO: 18 is the nucleic acid sequence of LJS142.

SEQ ID NO: 19 is the amino acid sequence of LJL17.
SEQ ID NO: 20 is the nucleic acid sequence of LJL17.
SEQ ID NO: 21 is the amino acid sequence of LJM06.
SEQ ID NO: 22 is the nucleic acid sequence of LJM06.
SEQ ID NO: 23 is the amino acid sequence of LJM17.
SEQ ID NO: 24 is the nucleic acid sequence of LJM17.
SEQ ID NO: 25 is the amino acid sequence of LJL04.
SEQ ID NO: 26 is the nucleic acid sequence of LJL04.
SEQ ID NO: 27 is the amino acid sequence of LJM114.
SEQ ID NO: 28 is the nucleic acid sequence of LJM114.
SEQ ID NO: 29 is the amino acid sequence of LJM111.
SEQ ID NO: 30 is the nucleic acid sequence of LJM111.
SEQ ID NO: 31 is the amino acid sequence of LJM78.
SEQ ID NO: 32 is the nucleic acid sequence of LJM78.
SEQ ID NO: 33 is the amino acid sequence of LJS238.
SEQ ID NO: 34 is the nucleic acid sequence of LJS238.
SEQ ID NO: 35 is the amino acid sequence of LJS169.
SEQ ID NO: 36 is the nucleic acid sequence of LJS169.
SEQ ID NO: 37 is the amino acid sequence of LJL11.
SEQ ID NO: 38 is the nucleic acid sequence of LJL11.
SEQ ID NO: 39 is the amino acid sequence of LJL08.
SEQ ID NO: 40 is the nucleic acid sequence of LJL08.
SEQ ID NO: 41 is the amino acid sequence of LJS105.
SEQ ID NO: 42 is the nucleic acid sequence of LJS105.
SEQ ID NO: 43 is the amino acid sequence of LJL09.
SEQ ID NO: 44 is the nucleic acid sequence of LJL09.
SEQ ID NO: 45 is the amino acid sequence of LJL38.
SEQ ID NO: 46 is the nucleic acid sequence of LJL38.
SEQ ID NO: 47 is the amino acid sequence of LJM04.
SEQ ID NO: 48 is the nucleic acid sequence of LJM04.
SEQ ID NO: 49 is the amino acid sequence of LJM26.
SEQ ID NO: 50 is the nucleic acid sequence of LJM26.
SEQ ID NO: 51 is the amino acid sequence of LJS03.
SEQ ID NO: 52 is the nucleic acid sequence of LJS03.
SEQ ID NO: 53 is the amino acid sequence of LJS192.
SEQ ID NO: 54 is the nucleic acid sequence of LJS192.
SEQ ID NO: 55 is the amino acid sequence of LJM19.
SEQ ID NO: 56 is the nucleic acid sequence of LJM19.
SEQ ID NO: 57 is the amino acid sequence of LJL138.

SEQ ID NO: 58 is the nucleic acid sequence of LJL138.
SEQ ID NO: 59 is the amino acid sequence of LJL15.
SEQ ID NO: 60 is the nucleic acid sequence of LJL15.
SEQ ID NO: 61 is the amino acid sequence of LJL91.
SEQ ID NO: 62 is the nucleic acid sequence of LJL91.
SEQ ID NO: 63 is the amino acid sequence of LJM11.
SEQ ID NO: 64 is the nucleic acid sequence of LJM11.
SEQ ID NO: 65 is the amino acid sequence of LJS138.
SEQ ID NO: 66 is the nucleic acid sequence of LJS138.
SEQ ID NO: 67 is the amino acid sequence of LJL124.
SEQ ID NO: 68 is the nucleic acid sequence of LJL124.
SEQ ID NO: 69 is the amino acid sequence of LJL35.
SEQ ID NO: 70 is the nucleic acid sequence of LJL35.
SEQ ID NO: 71 is an oligonucleotide primer.
SEQ ID NO: 72 is an oligonucleotide primer.
SEQ ID NO: 73 is an oligonucleotide primer.

DETAILED DESCRIPTION

I. Abbreviations

AAV	adeno-associated virus
AcNPV	Autographa California Nuclear Polyhedrosis Virus
alum	aluminum phosphate or aluminum hydroxide
BCG	Bacillus Calmette Guerin
BLAST	Basic Local Alignment Search Tool
BSA	bovine serum albumin
CAV	canine adenovirus
CDR	complementarity determining region
CHV	canine herpes virus
CMV	cytomegalovirus
CTL	cytotoxic T lymphocyte
DMRIE	N-(2-hydroxyethyl)-N,N-diméthyl-2,3-bis(tetradecyloxy)-1-propanammonium
DOPE	dioleoyl-phosphatidyl-ethanolamine
DTH	delayed type hypersensitivity
fMLP	N-formyl-methionyl-leucyl-phenylalanine
GM-CSF	granulocyte-macrophage colony stimulating factor
H	heavy chains

HLB	hydrophile-lipophile balance
ID	intradermal
IM	intramuscular
ISS	immunostimulating sequence
KLH	keyhole limpet hemocyanin
L	light chains
LB	Luria broth
Lu. longipalpis	*Lutzomyia logipalpis*
MVA	Modified Vaccinia virus Ankara
OFR	open reading frame
P. ariasi	*Phlebotomus ariasi*
PCR	polymerase chain reaction
polyA	polyadenylation signal
P. papatasi	*Phlebotomus papatasi*
PVDF	polyvinylidene difluoride
SC	subcutaneous
SCA	Single chain antibody
sFv	single-chain antigen binding proteins
SGH	salivary gland homogenate
SPGA	sucrose phosphate glutamate albumin
tPA	tissue plasminogen activator
V_H	variable region of the heavy chain
V_L	variable region of the light chain
VL	visceral leishmaniasis

II. Terms

Unless otherwise noted, technical terms are used according to conventional usage. Definitions of common terms in molecular biology may be found in Benjamin Lewin, *Genes V*, published by Oxford University Press, 1994 (ISBN 0-19-854287-9); Kendrew *et al.* (eds.), *The Encyclopedia of Molecular Biology*, published by Blackwell Science Ltd., 1994 (ISBN 0-632-02182-9); and Robert A. Meyers (ed.), *Molecular Biology and Biotechnology: a Comprehensive Desk Reference*, published by VCH Publishers, Inc., 1995 (ISBN 1-56081-569-8).

In order to facilitate review of the various embodiments of the disclosure, the following explanations of specific terms are provided:

Amplification of a nucleic acid molecule (for example, a DNA or RNA molecule): A technique that increases the number of copies of a nucleic acid molecule in a specimen. An example of amplification is the polymerase chain reaction, in which a biological sample collected from a

subject is contacted with a pair of oligonucleotide primers, under conditions that allow for the hybridization of the primers to a nucleic acid template in the sample. The primers are extended under suitable conditions, dissociated from the template, and then re-annealed, extended, and dissociated to amplify the number of copies of the nucleic acid. The product of amplification may be characterized by electrophoresis, restriction endonuclease cleavage patterns, oligonucleotide hybridization or ligation, and/or nucleic acid sequencing using standard techniques. Other examples of amplification include strand displacement amplification, as disclosed in U.S. Patent No. 5,744,311; transcription-free isothermal amplification, as disclosed in U.S. Patent No. 6,033,881; repair chain reaction amplification, as disclosed in WO 90/01069; ligase chain reaction amplification, as disclosed in EP 0320308; gap filling ligase chain reaction amplification, as disclosed in U.S. Patent No. 5,427,930; and NASBA™ RNA transcription-free amplification, as disclosed in U.S. Patent No. 6,025,134.

Antibody: immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, for instance, molecules that contain an antigen binding site that specifically binds (immunoreacts with) an antigen.

A naturally occurring antibody (for example, IgG, IgM, IgD) includes four polypeptide chains, two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds. However, it has been shown that the antigen-binding function of an antibody can be performed by fragments of a naturally occurring antibody. Thus, these antigen-binding fragments are also intended to be designated by the term "antibody." Specific, non-limiting examples of binding fragments encompassed within the term antibody include (i) an Fab fragment consisting of the V_L, V_H, CL, and CH1 domains; (ii) an Fd fragment consisting of the V_H and CH1 domains; (iii) an Fv fragment consisting of the V_L and V_H domains of a single arm of an antibody, (iv) a dAb fragment (Ward *et al.*, *Nature* 341:544-546, 1989) which consists of a V_H domain; (v) an isolated complimentarity determining region (CDR); and (vi) an $F(ab')_2$ fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region.

Immunoglobulins and certain variants thereof are known and many have been prepared in recombinant cell culture (for example, see U.S. Patent No. 4,745,055; U.S. Patent No. 4,444,487; WO 88/03565; EP 0256654; EP 0120694; EP 0125023; Faoulkner *et al.*, *Nature* 298:286, 1982; Morrison, *J. Immunol.* 123:793, 1979; Morrison *et al.*, *Ann Rev. Immunol* 2:239, 1984).

Animal: Living multi-cellular vertebrate organisms, a category that includes, for example, mammals and birds. The term mammal includes both human and non-human mammals. Similarly, the term "subject" includes both human and veterinary subjects, such as dogs.

Conservative variants: Conservative amino acid substitutions are those substitutions that do not substantially affect or decrease an activity or antigenicity of the *Lu. longipalpis* polypeptide. Specific, non-limiting examples of a conservative substitution include the following examples:

Original Residue	Conservative Substitutions
Ala	Ser
Arg	Lys
Asn	Gln, His
Asp	Glu
Cys	Ser
Gln	Asn
Glu	Asp
His	Asn; Gln
Ile	Leu, Val
Leu	Ile; Val
Lys	Arg; Gln; Glu
Met	Leu; Ile
Phe	Met; Leu; Tyr
Ser	Thr
Thr	Ser
Trp	Tyr
Tyr	Trp; Phe
Val	Ile; Leu

The term conservative variation also includes the use of a substituted amino acid in place of an unsubstituted parent amino acid, provided that antibodies raised to the unsubstituted polypeptide also essentially immunoreact with the substituted polypeptide, or that an immune response can be generated against the substituted polypeptide that is similar to the immune response against the unsubstituted polypeptide. Thus, in one embodiment, non-conservative substitutions are those that reduce an activity or antigenicity.

cDNA (complementary DNA): A piece of DNA lacking internal, non-coding segments (introns) and expression control sequences. cDNA is synthesized in the laboratory by reverse transcription from messenger RNA extracted from cells.

Degenerate variant: A polynucleotide encoding a *Lu. longipalpis* polypeptide that includes a sequence that is degenerate as a result of the genetic code. There are 20 natural amino acids, most of which are specified by more than one codon. Therefore, all degenerate nucleotide sequences are included in the disclosure as long as the amino acid sequence of the *Lu. longipalpis* polypeptide encoded by the nucleotide sequence is unchanged.

Delayed-type hypersensitivity (DTH): An immune reaction in which T cell-dependent macrophage activation and inflammation cause tissue injury. A DTH reaction to the subcutaneous injection of antigen is often used as an assay for cell-mediated immunity.

Epitope: An antigenic determinant. These are particular chemical groups or peptide sequences on a molecule that are antigenic, for instance, that elicit a specific immune response. An antibody specifically binds a particular antigenic epitope on a polypeptide. Specific, non-limiting examples of an epitope include a tetra- to penta-peptide sequence in a polypeptide, a tri- to penta-glycoside sequence in a polysaccharide. In the animal most antigens will present several or even many antigenic determinants simultaneously. Such a polypeptide may also be qualified as an immunogenic polypeptide and the epitope may be identified as described further.

Expression Control Sequences: Nucleic acid sequences that control and regulate the expression of a nucleic acid sequence, such as a heterologous nucleic acid sequence, to which it is operably linked. Expression control sequences are operably linked to a nucleic acid sequence when the expression control sequences control and regulate the transcription and, as appropriate, translation of the nucleic acid sequence. Thus expression control sequences can include appropriate promoters, enhancers, transcription terminators, polyA signals, a start codon (for instance, ATG) in front of a protein-encoding polynucleotide sequence, splicing signal for introns, maintenance of the correct reading frame of that gene to permit proper translation of mRNA, and stop codons. The term "control sequences" is intended to include, at a minimum, components whose presence can influence expression, and can also include additional components whose presence is advantageous, for example, leader sequences and fusion partner sequences. Expression control sequences can include a promoter.

A promoter is a minimal sequence sufficient to direct transcription of a nucleic acid. Promoters may be cell-type specific or tissue specific. A promoter includes necessary nucleic acid sequences near the start site of transcription, such as, in the case of a polymerase II type promoter, a TATA element. A promoter also optionally includes distal enhancer or repressor elements which can be located as much as several thousand base pairs from the start site of transcription. Both constitutive and inducible promoters are included (see for example, Bitter *et al., Methods in Enzymology* 153:516-544, 1987).

For example, when cloning in bacterial systems, inducible promoters such as pL of bacteriophage lambda, plac, ptrp, ptac (ptrp-lac-hybrid promoter) and the like may be used. In one embodiment, when cloning in mammalian cell systems, promoters derived from the genome of mammalian cells (for example, metallothionein promoter) or from mammalian viruses (for example, the retrovirus long terminal repeat; the adenovirus late promoter; the vaccinia virus 7.5K promoter) can be used. Promoters produced by recombinant DNA or synthetic techniques may also be used to provide for transcription of the nucleic acid sequences. A polynucleotide can be inserted into an expression vector that contains a promoter sequence which facilitates the efficient transcription of the inserted genetic sequence of the host. The expression vector typically contains an origin of replication, a promoter, as well as specific nucleic acid sequences that allow phenotypic selection of the transformed cells. In one embodiment, the promoter is a cytomegalovirus promoter.

Host cells: Cells in which a vector can be propagated and its DNA expressed. The cell may be prokaryotic or eukaryotic. The term also includes any progeny of the subject host cell. It is understood that all progeny may not be identical to the parental cell since there may be mutations that occur during replication. However, such progeny are included when the term "host cell" is used. Also includes the cells of the subject.

Immune response: A response of a cell of the immune system, such as a B cell, T cell, or monocyte, to a stimulus. In one embodiment, the response is specific for a particular antigen (an "antigen-specific response"). The response can also be a non-specific response (not targeted specifically to salivary polypeptides) such as production of lymphokines. In one embodiment, an

immune response is a T cell response, such as a CD4+ response or a CD8+ response. In another embodiment, the response is a Th1 (a subset of helper T cells) response. In yet another embodiment, the response is a B cell response, and results in the production of specific antibodies.

Immunogenic polypeptide: A polypeptide which comprises an allele-specific motif, an epitope or other sequence such that the polypeptide will bind an MHC molecule and induce a cytotoxic T lymphocyte ("CTL") response, and/or a B cell response (for example, antibody production), and/or T-helper lymphocyte response, and/or a delayed type hypersensitivity (DTH) response against the antigen from which the immunogenic polypeptide is derived.

In one embodiment, immunogenic polypeptides are identified using sequence motifs or other methods known in the art. Typically, algorithms are used to determine the "binding threshold" of polypeptides to select those with scores that give them a high probability of binding at a certain affinity and will be immunogenic. The algorithms are based either on the effects on MHC binding of a particular amino acid at a particular position, the effects on antibody binding of a particular amino acid at a particular position, or the effects on binding of a particular substitution in a motif-containing polypeptide. Within the context of an immunogenic polypeptide, a "conserved residue" is one which appears in a significantly higher frequency than would be expected by random distribution at a particular position in a polypeptide. In one embodiment, a conserved residue is one where the MHC structure may provide a contact point with the immunogenic polypeptide.

Immunogenic composition: A composition that, when administered to a subject induces an immune response to a *Lu. longipalpis* salivary polypeptide. In one embodiment, in particular a positive DTH response.

Isolated: An "isolated" biological component (such as a nucleic acid or protein or organelle) has been substantially separated or purified away from other biological components in the cell of the organism in which the component naturally occurs, for instance, other chromosomal and extra-chromosomal DNA and RNA, proteins, and organelles. Nucleic acids and proteins that have been "isolated" include nucleic acids and proteins purified by standard purification methods. The term also embraces nucleic acids and proteins prepared by recombinant technology as well as chemical synthesis.

Label: A detectable compound or composition that is conjugated directly or indirectly to another molecule to facilitate detection of that molecule. Specific, non-limiting examples of labels include fluorescent tags, enzymatic linkages, and radioactive isotopes.

Leishmaniasis: A parasitic disease spread by the bite of infected sand flies. The trypanosomatid parasite of the genus *Leishmania* is the etiological agent of a variety of disease manifestations, which are collectively known as leishmaniasis. Leishmaniasis is prevalent through out the tropical and sub-tropical regions of Africa, Asia, the Mediterranean, Southern Europe (old world), and South and Central America (new world). The old world species are transmitted by the sand fly vector *Phlebotomus sp.* Humans, wild animals and domestic animals (such as dogs) are known to be targets of these sand flies and to act as reservoir hosts or to develop leishmaniasis.

Cutaneous leishmaniasis starts as single or multiple nodules that develop into ulcers in the skin at the site of the bite. The chiclero ulcer typically appears as a notch-like loss of tissue on the ear lobe. The incubation period ranges from days to months, even a year in some cases. The sores usually last months to a few years, with most cases healing on their own. The mucocutaneous type can develop into erosive lesions in the nose, mouth, or throat and can lead to severe disfigurement. Visceral leishmaniasis often has fever occurring in a typical daily pattern, abdominal enlargement with pain, weakness, widespread swelling of lymph nodes, and weight loss, as well as superimposed infections because of a weakened immune system. Visceral leishmaniasis (VL) can result in high death rates. The onset of symptoms can be sudden, but more often tends to be insidious.

***Lutzomyia longipalpis* (*Lu. longipalpis*):** A species of sand fly endogenous to the New World (South and Central America). This sand fly is the principal vector of American visceral leishmaniasis, a potentially fatal disease that primarily affects children in several countries of South and Central America.

Lymphocytes: A type of white blood cell that is involved in the immune defenses of the body. There are two main types of lymphocytes: B cells and T cells.

Mammal: This term includes both human and non-human mammals. Similarly, the term "subject" includes both human and veterinary subjects.

Oligonucleotide: A linear polynucleotide sequence of up to about 100 nucleotide bases in length.

Open reading frame (ORF): A nucleic acid sequence having a series of nucleotide triplets (codons), starting with a start codon and ending with a stop codon, coding for amino acids without any internal termination codons. These sequences are usually translatable into a polypeptide.

Operably linked: A first nucleic acid sequence is operably linked with a second nucleic acid sequence when the first nucleic acid sequence is placed in a functional relationship with the second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding sequence. Generally, operably linked DNA sequences are contiguous and, where necessary to join two protein-coding regions, in the same reading frame.

Polypeptide Modifications: *Lu. longipalpis* polypeptides include synthetic embodiments of polypeptides described herein. In addition, analogues (non-peptide organic molecules), derivatives (chemically functionalized peptide molecules obtained starting with the disclosed polypeptide sequences) and variants (homologs) of these proteins can be utilized in the methods described herein. Each polypeptide of the disclosure is comprised of a sequence of amino acids, which may be either L- and/or D- amino acids, naturally occurring and otherwise.

Polypeptides may be modified by a variety of chemical techniques to produce derivatives having essentially the same activity as the unmodified polypeptides, and optionally having other desirable properties. For example, carboxylic acid groups of the protein, whether carboxyl-terminal or side chain, may be provided in the form of a salt of a pharmaceutically-acceptable cation or esterified to form a C_1-C_{16} ester, or converted to an amide of formula NR_1R_2 wherein R_1 and R_2 are

each independently H or C_1-C_{16} alkyl, or combined to form a heterocyclic ring, such as a 5- or 6-membered ring. Amino groups of the peptide, whether amino-terminal or side chain, may be in the form of a pharmaceutically-acceptable acid addition salt, such as the HCl, HBr, acetic, benzoic, toluene sulfonic, maleic, tartaric, and other organic salts, or may be modified to C_1-C_{16} alkyl or dialkyl amino or further converted to an amide.

Hydroxyl groups of the peptide side chains may be converted to C_1-C_{16} alkoxy or to a C_1-C_{16} ester using well-recognized techniques. Phenyl and phenolic rings of the peptide side chains may be substituted with one or more halogen atoms, such as fluorine, chlorine, bromine, or iodine, or with C_1-C_{16} alkyl, C_1-C_{16} alkoxy, carboxylic acids and esters thereof, or amides of such carboxylic acids. Methylene groups of the peptide side chains can be extended to homologous C_2-C_4 alkylenes. Thiols can be protected with any one of a number of well-recognized protecting groups, such as acetamide groups. Those skilled in the art will also recognize methods for introducing cyclic structures into the peptides of this disclosure to select and provide conformational constraints to the structure that result in enhanced stability.

Peptidomimetic and organomimetic embodiments are envisioned, whereby the three-dimensional arrangement of the chemical constituents of such peptido- and organomimetics mimic the three-dimensional arrangement of the peptide backbone and component amino acid side chains, resulting in such peptido- and organomimetics of a *L. longipalpis* polypeptide having measurable or enhanced ability to generate an immune response. For computer modeling applications, a pharmacophore is an idealized, three-dimensional definition of the structural requirements for biological activity. Peptido- and organomimetics can be designed to fit each pharmacophore with current computer modeling software (using computer assisted drug design or CADD). See Walters, "Computer-Assisted Modeling of Drugs," Klegerman & Groves (eds.), 1993, *Pharmaceutical Biotechnology*, Interpharm Press: Buffalo Grove, IL, pp. 165-174 and *Principles of Pharmacology* Munson (ed.) 1995, Ch. 102, for descriptions of techniques used in CADD. Also included are mimetics prepared using such techniques.

Pharmaceutically acceptable vehicles or excipients: The pharmaceutically acceptable vehicles or excipients of use are conventional. *Remington's Pharmaceutical Sciences*, by E. W. Martin, Mack Publishing Co., Easton, PA, 15th Edition (1975), describes compositions and formulations suitable for pharmaceutical delivery of the polypeptides, plasmids, viral vectors herein disclosed.

In general, the nature of the vehicle or excipient will depend on the particular mode of administration being employed. For instance, parenteral formulations usually comprise injectable fluids that include pharmaceutically and physiologically acceptable fluids such as water, physiological saline, balanced salt solutions, aqueous dextrose, glycerol or the like as a vehicle. For solid compositions (for example, freeze-dried pastille, powder, pill, tablet, or capsule forms), conventional non-toxic solid vehicles or excipients can include, for example, pharmaceutical grades of mannitol, lactose, starch, or magnesium stearate. In addition to biologically neutral vehicles or excipients, immunogenic compositions to be administered can contain minor amounts of non-toxic

auxiliary substances, such as wetting or emulsifying agents, preservatives, and pH buffering agents and the like, for example sodium acetate or sorbitan monolaurate.

Phlebotomus ariasi (P. ariasi): A species of Phlebotomus (sand flies) genus endogenous to the Old World, in particular to southern Europe and Mediterranean countries, more particularly to Spain and France. This sand fly is a proven vector of visceral leishmaniasis. *P. ariasi* is a member of the subgenera of Phlebotomus Larroussius.

***Phlebotomus perniciosus* (*P. perniciosus*):** A species of Phlebotomus (sand flies) genus endogenous to the Old World, in particular to southern Europe, and Mediterranean countries, more particularly to France, Italy, Greece, Morocco, and Spain. This sand fly is a proven vector of the visceral leishmaniasis. *P. perniciosus* is a member of the subgenera of Phlebotomus Larroussius.

Polynucleotide: The term polynucleotide or nucleic acid sequence refers to a polymeric form of nucleotide at least 10 bases in length, thus including oligonucleotides and genes. A recombinant polynucleotide includes a polynucleotide that is not immediately contiguous with both of the coding sequences with which it is immediately contiguous (one on the 5' end and one on the 3' end) in the naturally occurring genome of the organism from which it is derived. The term therefore includes, for example, a recombinant DNA which is incorporated into a vector; into an autonomously replicating plasmid or virus; or into the genomic DNA of a prokaryote or eukaryote, or which exists as a separate molecule (for example, a cDNA) independent of other sequences. The polynucleotides can be ribonucleotides, deoxyribonucleotides, or modified forms of either nucleotide. The term includes single -and double -stranded forms of DNA.

Polypeptide: Any chain of amino acids, regardless of length (thus encompassing oligopeptides, peptides, and proteins) or post-translational modification (for example, glycosylation, phosphorylation, or acylation). A polypeptide encompasses also the precursor, as well as the mature protein. In one embodiment, the polypeptide is a polypeptide isolated from *Lu. longipalpis*, or encoded by a nucleic acid isolated from *Lu. longipalpis*, such as the *Lu. longipalpis* polypeptides disclosed herein.

Probes and primers: A probe comprises an isolated polynucleotide attached to a detectable label or reporter molecule. Primers are short polynucleotides. In one embodiment, polynucleotides are 15 nucleotides or more in length. Primers may be annealed to a complementary target DNA strand by nucleic acid hybridization to form a hybrid between the primer and the target DNA strand, and then extended along the target DNA strand by a DNA polymerase enzyme. Primer pairs can be used for amplification of a nucleic acid sequence, for example, by the polymerase chain reaction (PCR) or other nucleic-acid amplification methods known in the art. One of skill in the art will appreciate that the specificity of a particular probe or primer increases with its length. Thus, for example, a primer comprising 20 consecutive nucleotides will anneal to a target with a higher specificity than a corresponding primer of only 15 nucleotides. Thus, in order to obtain greater specificity, probes and primers may be selected that comprise at least 15, 20, 25, 30, 35, 40, 50 or more consecutive nucleotides.

Protein Purification: The *Lu. longipalpis* polypeptides disclosed herein can be purified by any of the means known in the art. See, for example, *Guide to Protein Purification*, Deutscher (ed.), *Meth. Enzymol.* 185, Academic Press, San Diego, 1990; and Scopes, *Protein Purification: Principles and Practice*, Springer Verlag, New York, 1982. Substantial purification denotes purification from other proteins or cellular components. A substantially purified protein is at least 60%, 70%, 80%, 90%, 95%, or 98% pure. Thus, in one specific, non-limiting example, a substantially purified protein is 90% free of other proteins or cellular components.

Purified: The term purified does not require absolute purity; rather, it is intended as a relative term. Thus, for example, a purified polypeptide preparation is one in which the polypeptide is more enriched than the polypeptide is in its natural environment. A polypeptide preparation is substantially purified such that the polypeptide represents several embodiments at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, or at least 98%, of the total polypeptide content of the preparation. The same applies for polynucleotides. The polypeptides disclosed herein can be purified by any of the means known in the art (see, for example, *Guide to Protein Purification*, Deutscher (ed.), *Meth. Enzymol.* 185, Academic Press, San Diego, 1990; and Scopes, *Protein Purification: Principles and Practice*, Springer Verlag, New York, 1982).

Recombinant: A recombinant polynucleotide is one that has a sequence that is not naturally occurring or has a sequence that is made by an artificial combination of two otherwise separated segments of sequence. This artificial combination is often accomplished by chemical synthesis or, more commonly, by the artificial manipulation of isolated segments of nucleic acids, for example, by genetic engineering techniques. In one embodiment, a recombinant polynucleotide encodes a fusion protein.

Selectively hybridize: Hybridization under moderately or highly stringent conditions that excludes non-related nucleotide sequences.

In nucleic acid hybridization reactions, the conditions used to achieve a particular level of stringency will vary, depending on the nature of the nucleic acids being hybridized. For example, the length, degree of complementarity, nucleotide sequence composition (for example, GC v. AT content), and nucleic acid type (for example, RNA v. DNA) of the hybridizing regions of the nucleic acids can be considered in selecting hybridization conditions. An additional consideration is whether one of the nucleic acids is immobilized, for example, on a filter.

A specific, non-limiting example of progressively higher stringency conditions is as follows: 2 x SSC/0.1% SDS at about room temperature (hybridization conditions); 0.2 x SSC/0.1% SDS at about room temperature (low stringency conditions); 0.2 x SSC/0.1% SDS at about 42°C (moderate stringency conditions); and 0.1 x SSC at about 68°C (high stringency conditions). One of skill in the art can readily determine variations on these conditions (for example, *Molecular Cloning: A Laboratory Manual*, 2nd ed., vol. 1-3, ed. Sambrook *et al.*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989). The hydridization conditions can be carried out over 2 to 16 hours. Washing can be carried out using only one of the above conditions, for example, high stringency

conditions, or each of the conditions can be used, for example, for 10-15 minutes each, in the order listed above, repeating any or all of the steps listed. However, as mentioned above, optimal conditions will vary, depending on the particular hybridization reaction involved, and can be determined empirically.

Sequence identity: The similarity between amino acid sequences is expressed in terms of the percentage identity between the sequences. The higher the percentage, the more similar the two sequences are. Homologs or variants of a *Lu. longipalpis* polypeptide will possess a relatively significant high degree of sequence identity when aligned using standard methods.

Methods of alignment of sequences for comparison are well known in the art. Various programs and alignment algorithms are described in: Smith and Waterman, *Adv. Appl. Math.* 2:482, 1981; Needleman and Wunsch, *J. Mol. Biol.* 48:443, 1970; Pearson and Lipman, *Proc. Natl. Acad. Sci. USA* 85:2444, 1988; Higgins and Sharp, *Gene* 73:237, 1988; Higgins and Sharp, *CABIOS* 5:151, 1989; Corpet *et al.*, *Nucleic Acids Research* 16:10881, 1988; and Pearson and Lipman, *Proc. Natl. Acad. Sci. USA* 85:2444, 1988. Altschul *et al.*, *Nature Genet.* 6:119, 1994 presents a detailed consideration of sequence alignment methods and identity calculations.

The NCBI Basic Local Alignment Search Tool (BLAST) (Altschul *et al.*, *J. Mol. Biol.* 215:403, 1990) is available from several sources, including the National Center for Biotechnology Information (NCBI, Bethesda, MD) and on the Internet, for use in connection with the sequence analysis programs blastp, blastn, blastx, tblastn, and tblastx. A description of how to determine sequence identity using this program is available on the NCBI website on the internet.

Homologs and variants of a *Lu. longipalpis* polypeptide are typically characterized by possession of at least 75%, for example at least 80%, sequence identity counted over the full length alignment with the amino acid sequence of the *Lu. longipalpis* polypeptide using the NCBI Blast 2.0, gapped blastp set to default parameters. The comparison between the sequences is made over the full length alignment with the amino acid sequence given in this present disclosure, employing the Blast 2 sequences function using the default BLOSUM62 matrix set to default parameters, (gap existence cost of 11, and a per residue gap cost of 1).

When aligning short peptides (fewer than around 30 amino acids), the alignment should be performed using the Blast 2 sequences function, employing the PAM30 matrix set to default parameters (open gap 9, extension gap 1 penalties). Proteins with even greater similarity to the reference sequences will show increasing percentage identities when assessed by this method, such as at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% sequence identity. When less than the entire sequence is being compared for sequence identity, homologues and, variants will typically possess at least 80% sequence identity over short windows of 10-20 amino acids, and may possess sequence identities of at least 85% or at least 90% or 95% depending on their similarity to the reference sequence. Methods for determining sequence identity over such short windows are available at the NCBI website on the internet. One of skill in the art will appreciate that these sequence identity ranges are provided for guidance only; it is entirely possible that strongly significant homologues could be obtained that fall outside of the ranges provided.

Specific binding agent: An agent that binds substantially only to a defined target. Thus a *Lu. longipalpis* specific binding agent is an agent that binds substantially to a *Lu. longipalpis* polypeptide.

In one embodiment, the specific binding agent is a monoclonal or polyclonal antibody that specifically binds the *Lu. longipalpis* polypeptide.

Subject: Living multi-cellular vertebrate organisms, a category that includes both human veterinary subjects, including human and non-human mammals. In one embodiment, the subject is a member of the canine family, such as a dog. In another embodiment, the subject is a human.

T Cell: A white blood cell critical to the immune response. T cells include, but are not limited to, $CD4^+$ T cells and $CD8^+$ T cells. A $CD4^+$ T lymphocyte is an immune cell that carries a marker on its surface known as "cluster of differentiation 4" (CD4). These cells, also known as helper T cells, help orchestrate the immune response, including antibody responses as well as killer T cell responses. $CD8^+$ T cells carry the "cluster of differentiation 8" (CD8) marker. In one embodiment, a CD8 T cells is a cytotoxic T lymphocytes. In another embodiment, a CD8 cell is a suppressor T cell.

Therapeutically active polypeptide: An agent, such as a *Lu. longipalpis* polypeptide, that causes induction of an immune response, as measured by clinical response (for example, increase in a population of immune cells, production of antibody that specifically binds the *Lu. longipalpis* polypeptide, a measurable reduction in symptoms resulting from exposure to *Leishmania*, or protection from infection with *Leishmania*). Therapeutically active molecules can also be made from nucleic acids. Examples of a nucleic acid based therapeutically active molecule is a nucleic acid sequence that encodes a *Lu. longipalpis* polypeptide, wherein the nucleic acid sequence is operably linked to a control element such as a promoter. Therapeutically active agents can also include organic or other chemical compounds that mimic the effects of the *Lu. longipalpis* polypeptide.

The terms "therapeutically effective fragment of a *Lu. longipalpis* polypeptide" includes any fragment of the *Lu. longipalpis* polypeptide, or variant of the *Lu. longipalpis* polypeptide, or fusion protein including a *Lu. longipalpis* polypeptide, that retains a function of the *Lu. longipalpis* polypeptide (such as immunogenicity), or retains the ability to reduce the symptoms from exposure to *Leishmania,* or to protect from infection with *Leishmania.*

Thus, in one embodiment, a therapeutically effective amount of a fragment of *Lu. longipalpis* polypeptide is an amount used to generate an immune response to the polypeptide. In another embodiment, a therapeutically effective amount of a fragment of a *Lu. longipalpis* polypeptide is an amount of use to prevent or treat a *Leishmania* infection in a subject. Treatment refers to a therapeutic intervention that confers resistance to infection with *Leishamania*, or a reduction in the symptoms associated with exposure to *Leishamania*. Specific, non-limiting examples of a polypeptide fragment are the N-terminal half or the C-terminal half of one of the *P. Lu. longipalpis* polypeptide disclosed herein. It should be noted that fusion proteins are included, such as a fusion with six histidine residues, a c-myc tag, or any other polypeptide tag. Such fusions are known to one of skill in the art, and are often used in protein purification.

Transduced: A transduced cell is a cell into which has been introduced a nucleic acid molecule by molecular biology techniques. As used herein, the term transduction encompasses all

techniques by which a nucleic acid molecule might be introduced into such a cell, including transfection with viral vectors, transformation with plasmid vectors, and introduction of naked DNA by electroporation, lipofection, and particle gun acceleration.

Vector: A nucleic acid molecule as introduced into a host cell, thereby producing a transduced host cell. A vector may include nucleic acid sequences that permit it to replicate in a host cell, such as an origin of replication. A vector may also include one or more selectable marker genes and other genetic elements known in the art.

Vaccine: Composition that when administered to a subject, induces a decrease of the severity of the symptoms of a disorder or disease. In one embodiment, a vaccine decreases the severity of the symptoms of leishmaniasis and/or decreases the parasitic load.

Unless otherwise explained, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. The singular terms "a," "an," and "the" include plural referents unless context clearly indicates otherwise. Similarly, the word "or" is intended to include "and" unless the context clearly indicates otherwise. "Comprise" means "include," and a composition that comprises a polypeptide includes that polypeptide. It is further to be understood that all base sizes or amino acid sizes, and all molecular weight or molecular mass values, given for polynucleotides or polypeptides are approximate, and are provided for description. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including explanations of terms, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Lu. longipalpis Polynucleotides and Polypeptides

Salivary polypeptides from sand fly species *Lu. longipalpis,* are disclosed herein.

LJL34 (SEQ ID NO: 1)
MLQIKHLLIFVGLLVVVNAQSNYCKQESCSSGGVERPHIGCKNSGDFSETCSGDAEIVKMDK
KKQNLLVKMHNRLRDRFARGAVPGFAPAAKMPMLKWNDELAKLAEYNVRTCKFAHDKC
RAIDVCPYAGQNLAQMMSYPTHRDLNYVLKNLTREWFWEYRWAKQSQLDNYVGGPGKD
NKQIGHFTAFVHEKTDKVGCAIARFTNEHNFKETLLACNYCYTNMMKERIYTQGKPCSQCQ
SKKCGPVYKNLCDPSEKVDPTPDVLKQWKHGK

LJL18 (SEQ ID NO:3)
MLLRSLFVLFLIFLTFCNAEEELIERKLTGKTIYISTIKLPWFQALNHCVKNGYTMVSIKTFEE
NKELLKELKRVIRTEDTQVWIGGLKHHQFANFRWVSDGSHVATASGYTNWAPGEPADSFY
YDQFCMAMLFRKDGAPWDDLNCWVKNLFVCEKRDD

LJS193 (SEQ ID NO:5)

MKLLQIIFSLFLVFFPTSNGALTGNESAANAAPLPVVLWHGMGDSCCFPFSLGSIKKLIEQQIP
GIHVVSLKIGKSLIEDYESGFFVHPDKQIQEVCESLQNDLTLANGFNAIGFSQGSQFLRGLVQR
CSSIQVRNLISIGGQHQGVFGLPYCPSLSRKTCEYFRKLLNYAAYEKWVQKLLVQATYWHD
PLNEDAYRTGSTFLADINNERQINNDYINNIRKLNRFVMVKFLNDSMVQPIESSFFGFYAPGT
DTEVLPLKQSKIYLEDRLGLQSVPIDYLECGGDHLQFTKEWFIKFIIPYLKQ

LJS201 (SEQ ID NO: 7)

MRNFAVVSLAVAVLLFCAWPINAEDNEEVGKAREKRGLKDAMEHFKNGFKELTKDFKLPS
LPSLPGFGKKPESGSSEDSGDKTEDTSGSKDDQSKDNTVEES

LJL13 (SEQ ID NO: 9)

MNFLLKIFSLLCLCGLGYSWQDVRNADQTLWAYRSCQKNPEDKDHVPQWRKFELPDDEKT
HCYVKCVWTRLGAYNENENVFKIDVITKQFNERGLEVPAGLDQELGGSTDGTCKAVYDKS
MKFFKSHFMDFRNAYYATYDGSDEWFSKNPDVKPKGTKVSEYCKNKDDGDCKHSCSMYY
YRLIDEDNLVIPFSNLPDYPEDKLEECRNEAKSANECKSSVIYQCLENADKSALDASLNIL
DEFSGRY

LJL23 (SEQ ID NO: 11)

MFLKWVVCAFATVFLVGVSQAAPPGVEWYHFGLIADMDKKSIASDKTTFNSVLKIDELRHN
TKTDQYIYVRSRVKKPVSTRYGFKGRGAELSEIVVFNNKLYTVDDKSGITFRITKDGKLFPW
VILADADGQRPDGFKGEWATIKDDTIYVGSTGMLKFTSSLWVKKITKDGVVTSHDWTDKY
RKILKALNMPNGFVWHEAVTWSPFRKQWVFMPRKCSRHPFSQELEERTGCNKIVTADENFN
DIQVIHIQDQPYNLASGFSSFRFIPGTKNERLLALRTVEQEDQVKTWAVVMDMKGTVLMYE
KELYDEKFEGLAFFGGIKKN

LJM10 (SEQ ID NO: 13)

MALKFLPVLLLSCFAMSTALQVTEKELSDGKKIFISKVELNWFEALDFCIHRGLTLLSIKSAK
ENVDVTKAIRAELNFDSKKLAHVWTGGIRHSQDKYFRWINDGTKVVKRVYTNWFTGEPNN
GYWKDEFCLEIYYKTEEGKWNDDKCHVKHHFVCQEKK

LJL143 (SEQ ID NO: 15)

MNSINFLSIVGLISFGFIVAVKCDGDEYFIGKYKEKDETLFFASYGLKRDPCQIVLGYKCSNN
QTHFVLNFKTNKKSCISAIKLTSYPKINQNSDLTKNLYCQTGGIGTDNCKLVFKKRKRQIAAN
IEIYGIPAKKCSFKDRYIGADPLHVDSYGLPYQFDQEHGWNVERYNIFKDTRFSTEVFYHKN
GLFNTQITYLAEEDSFSEAREITAKDIKKKFSIILPNEEYKRISFLDVYWFQETMRKKPKYPYIH
YNGECSNENKTCELVFDTDELMTYALVKVFTNPESDGSRLKEEDLGRG

LJS142 (SEQ ID NO: 17)
MAFSNTLFVLFVSFLTFCGADQTLIEKELTGRTVYISKIKLNWNDAFDYCIRNGLTFAKIKSA
EENTELSEKLKTVIRTEEFQVWIGGIEHHQDSSFRWVSDSQPITNKLGYKYTNWNTGEPTNY
QNNEYCLEILFRKEDGKWNDFPCSARHHFVCEKRTK

LJL17 (SEQ ID NO: 19)
MQNFLLVSLALAALMLCAEAKPYDFPLYQDLIQGVIQRESQAEREKRSPNEDYEKQFGDIVD
QIKEISFNVMKMPHFGSSDDNRDDGEYVDHHYGDEDDRDYDHY

LJM06 (SEQ ID NO: 21)
MKFYIFGVFLVSFLALCNAEDYDKVKLTGRTVYISRSKAPWFTALDNCNR
RFTFAMIKSQKENEELTNALLSVIKSDEENVWIGGLRHDLDDYFRWISFGTALSKTSYTNWA
PKEPTGRPHRTQNDEFCMQMSFKDGGKWSDNTCWRKRLYVCEKRD

LJM17 (SEQ ID NO: 23)
MRFFFVFLAIVLFQGIHGAYVEIGYSLRNITFDGLDTDDYNPKFNIPTGLAVDPEGYRLFIAIPR
RKPKVPYTVAELNMVMNPGFPVERAPSFEKFKKFNGEGKKDLVNVYQPVIDDCRRLWVLDI
GKVEYTGGDADQYPKGKPTLIAYDLKKDHTPEIHRFEIPDDLYSSQVEFGGFAVDVVNTKG
DCTESFVYLTNFKDNSLIVYDETQKKAWKFTDKTFEADKESTFSYSGEEQMKYKVGLFGIAL
GDRDEMGHRPACYIAGSSTKVYSVNTKELKTENGQLNPQLHGDRGKYTDAIALAYDPEHK
VLYFAESDSRQVSCWNVNMELKPDNTDVIFSSARFTFGTDILVDSKGMLWIMANGHPPVED
QEKIWKMRFVNRKIRIMKVDTERVFKYSRCNPNYKPPK
EIEV

LJL04 (SEQ ID NO: 25)
MIKEVFSLALLVALAQCANEIPINRQGKDYPVPIIDPNKSSSDDYFDDRFYPDIDDEGIAEAPK
DNRGKSRGGGAAGAREGRLGTNGAKPGQGGTRPGQGGTRPGQGGTRPGQGGTRPGQGGT
RPGQGRTKPAQGTTRPAQGTRNPGSVGTKEAQDASKQGQGKRRPGQVGGKRPGQANAPNA
GTRKQQKGSRGVGRPDLSRYKDAPAKFVFKSPDFSGEGKTPTVNYFRTKKKEHIVTRGSPN
DEFVLEILDGDPTGLGLKSETIGKDTRLVLENPNGNSIVARVKIYKNGYSG

LJM114 (SEQ ID NO: 27)
MNSVNTLILTLLFAIFLLVKRSQAFLPSDPSICVKNLVLDTGRTCEESEYFPDIKNVKNGKRVY
IVCTDSDAVDYKFYICFDMNRLSGPPYPEEEILRESTVTYAQIYELMTTETTETKKPKKKPKN
SKTDDPPAIRPGFSFRNSISV

LJM111 (SEQ ID NO: 29)
MKLFFFLYTFGLVQTIFGVEIKQGFKWNKILYEGDTSENFNPDNNILTAFAYDPESQKLFLTV
PRKYPETMYTLAEVDTEKNSFESGDTSPLLGKFSGHETGKELTSVYQPVIDECHRLWVVDVG

SVERNSDGTEGQPEHNPTLVAYDLKEANYPEVIRYTFPDNSIEKPTFLGGFAVDVVKPDECSE
TFVYITNFLTNALIVYDHKNKDSWTVQDSTFGPDKKSKFDHDGQQYEYEAGIFGITLGERDN
EGNRQAYYLVASSTKLHSINTKELKQKGSKVNANYLGDRGESTDAIGLVYDPKTKTIFFVES
NSKRVSCWNTQETLNKDKIDVIYHNADFSFGTDISIDSQDNLWFLANGLPPLENSDKFVFTKP
RYQIFKVNIQEAIAGTKCEKNL

LJM78 (SEQ ID NO: 31)
MTFLIILGAFLLVQIITASALGLPEQFKGLEDLPKKPLAETYYHEGLNDGKTDEMVDIFKSLSD
EFKFSDENLDVGEEKNYKKRDITQNSVARNFLSNVKGIPSMPSLPSMPSMPSIPSLWSSQTQA
APNTALALPESDYSLLDMPNIVKNFLKETRDLYNDVGAFLKAITEALTNRSSSSQLLSSPMVS
TNKTKEFIRNEIQKVRKVRNFVQETLQKIRDISAAIAKKVKSSECLSNLTDIKGLVSDGINCLK
EKFNDGKRIILQLYNNLLKGLKIPNDLMVELKKCDTNQNNTLGRIICYFLTPLQLEKEQILLPV
EFIKRILELTHYFSTMKEDLINCGITTIASIT

LJS238 (SEQ ID NO:33)
MLKIVLFLSVLAVLVICVAAMPGSNVPWHISREELEKLREARKNHKALEKAIDELIDKYL

LJS169 (SEQ ID NO:35)
MKFSCPVFVAIFLLCGFYRVEGSSQCEEDLKEEAEAFFKDCNEAKANPGEYENLTKEEMFEE
LKEYGVADTDMETVYKLVEECWNELTTTDCKRFLEEAECFKKKNICKYFPDEVKLKKK

LJL11 (SEQ ID NO: 37)
MLFFLNFFVLVFSIELALLTASAAAEDGSYEIIILHTNDMHARFDQTNAGSNKCQEKDKIASK
CYGGFARVSTMVKKFREENGSSVLFLNAGDTYTGTPWFTLYKETIATEMMNILRPDAASLG
NHEFDKGVEGLVPFLNGVTFPILTANLDTSQEPTMTNAKNLKRSMIFTVSGHRVGVIGYLTP
DTKFLSDVGKVNFIPEVEAINTEAQRLKKEENAEIIIVVGHSGLIKDREIAEKCPLVDIIVGGHS
HTFLYTGSQPDREVPVDVYPVVVTQSSGKKVPIVQAYCFTKYLGYFKVTINGKGNVVGWTG
QPILLNNNIPQDQEVLTALEKYRERVENYGNRVIGVSRVILNGGHTECRFHECNMGNLITDA
FVYANVISTPMSTNAWTDASVVLYQSGGIRAPIDPRTAAGSITRLELDNVLPFGNALYVVKV
PGNVLRKALEHSVHRYSNTSGWGEFPQVSGLKIRFNVNEEIGKRVKSVKVLCSNCSQPEYQP
LRNKKTYNVIMDSFMKDGGDGYSMFKPLKIIKTLPLGDIETVEAYIEKMGPIFPAVEGRITV
LGGLQKSDEDWH

LJL08 (SEQ ID NO: 39)
MKQILLISLVVILAVLAFNVAEGCDATCQFRKAIEDCKKKADNSDVLQTSVQTTATFTSMDT
SQLPGNNVFKACMKEKAKEFRAGK

LJS105 (SEQ ID NO: 41)
MNVLFVSFTLTILLLCVKARPEDFVALQDQANFQKCLEQYPEPNQSGEVLACLKKREGAKD
FREKRSLDDIEGTFQESGN
LWGA

LJL09 (SEQ ID NO: 43)
MKITVILFTGFTIALVSSAVLKKNGETIEEEEVRAEQRLREINEELDRRKNINTVAAWAYASNI
TEVNLKNMNDVSVETAKYYKELASELKGFNAKEYKSEDLKRQIKKLSKLGYSALPSEKYKE
LLEAITWMESNYAKVKVCSYKDPKKCDLALEPEITEILIKSRDPEELKYYWKQWYDKAGTP
TRESFNKYVQLNREAAKLDGFYSGAESWLDEYEDETFEKQLEDIFAQIRPLYEQLHAYVRFK
LREKYGNDVVSEKGPIPMHLLGNMWGQTWSEVAPILVPYPEKKLLDVTDEMVKQGYTPIS
MFEKGDEFFQSLNMTKLPKTFWEYSILEKPQDGRELICHASAWDFYTKDDVRKQCTRVTMD
QFFTAHHELGHIQYYLQYQHLPSVYREGANPGFHEAVGDVLSLSVSSPKHLEKVGLLKDFKF
DEESQINQLLNLALDKMAFLPFAYTIDKYRWGVFRGEISPSEYNCKFWEMRSYYGGIEPPIAR
SESDFDPPAKYHISSDVEYLRYLVSFIIQFQFHQAVCQKTGQFVPNDPEKTLLNCDIYQSAEA
GNAFKEMLKLGSSKPWPDAMEILTGQRKMDASALIEYFRPLSEWLQKKNKELGAYVGWDK
STKCVKNVS

LJL38 (SEQ ID NO: 45)
MKTFALIFLALAVFVLCIDGAPTFVNLLDDVQEEVEVNTYEP

LJM04 (SEQ ID NO:47)
MNHLCFIIIALFFLVQQSLAEHPEEKCIRELARTDENCILHCTYSYYGFVDKNFRIAKKHVQKF
KKILVTFGAVPKKEKK
KLLEHIEACADSANADQPQTKDEKCTKINKYYRCVVDGKILPWNSYADAIIKFDKTLNV

LJM26 (SEQ ID NO: 49)
MKIIFLAAFLLADGIWAAEEPSVEIVTPQSVRRHATPKAQDARVGSESATTAPRPSESMDYW
ENDDFVPFEGPFKDIGEFDWNLSKIVFEENKGNAILSPLSVKLLMSLLFEASASGTLTQHQLR
QATPTIVTHYQSREFYKNIFDGLKKKSNDYTVHFGTRIYVDQFVTPRQRYAAILEKHYLTDL
KVEDFSKAKETTQAINSWVSNITNEHIKDLVKEEDVQNSVMLMLNAVYFRGLWRKPFNRTL
PLPFHVSADESKTTDFMLTDGLYYFYEAKELDAKILRIPYKGKQYAMTVILPNSKSGIDSFVR
QINTVLLHRIKWLMDEVECRVILPKFHFDMTNELKESLVKLGISQIFTSEASLPSLARGQGVQ
NRLQVSNVIQKAGIIVDEKGSTAYAASEVSLVNKFGDDEFVMFNANHPFLFTIEDETTGAILF
TGKVVDPTQ

LJS03 (SEQ ID NO: 51)
MRFLLLAFSVALVLSPTFAKPGLWDIVTGINDMVKNTANALKNRLTTSVTLFTNTITEAIKNA
NSSVSELLQQVNETLTDIINGVGQVQSAFVNSAGNVVVQIVDAAGNVLEVVVDEAGNIVEV
AGTALETIIPLPGVVIQKIIDALQGNAGTTSDSASSTVPQQS

LJS192 (SEQ ID NO: 53)
MVKYSCLVLVAIFLLAGPYGVVGSCENDLTEAAKYLQDECNAGEIADEFLPFSEEEVGEALS
DKPENVQEVTNIVRGCFEAEQAKEHGKCERFSALSQCYIEKNLCQFF

LJM19 (SEQ ID NO: 55)
MKFFYLIFSAIFFLADPALVKCSEDCENIFHDNAYLLKLDCEAGRVDPVEYDDISDEEIYEITV
DVGVSSEDQEKVAKIIRECIAQVSTQDCTKFSEIYDCYMKKKICNYYPENM

LJL138 (SEQ ID NO: 57)
MHLQLNLCAILLSVLNGIQGAPKSINSKSCAISFPENVTAKKEPVYLKPSNDGSLSTPLQPSGP
FVSLKIGESLAIFCPGDGKDVETITCNTNFDLASYSCNKSTSTDTIETEEVCGGSGKVYKVGFP
LPSGNFHSIYQTCFDKKNLTPLYSIHILNGQA
VGYHLKHTRGSFRTNGIYGKVNIDKLYKTQIEKFNKLFGPKQTFFRRPLNFLSRGHLSPEVDF
TFRREQHATEMYINTAPQYQSINQGNWLRVENHVRDLAKVLQKDITVVTGILGILRLKSKKI
EKEIYLGDDVIAVPAMFWKAVFDPQKQEAIVFVSSNNPHVKTFNPNCKDVCAQAGFGNDNL
EYFSNYSIGLTICCKLEEFVKRNKIILPKEVNNKNYTKKLLKFPKTRNKEGDKKVVRKRAKG
A

LJL15 (SEQ ID NO: 59)
MNLHLAIILFVSYFTLITATDLIEKELSDCKKIFISKAELTWFQALDFCTEQNLTLLSIKSAREN
DEVTKAVRAEVHLPDTKKSHIWLGGIRYDQDKDFRWISDGTTVTKTVYINWYQGEPNGGR
YQKEFCMELYFKTPAGQWNDDICTAKHHFICQEKK

LJL91 (SEQ ID NO: 61)
MNLPLAIILFVSYFTLITAADLTEKELSDGKKIFISKAELSWFDALDACTEKDLTLLTIKSAREN
EEVTKAVRAEVHLPDTKKSHIWLGGIRYDQDKDFRWISDGTTVTKTVYINWYQGEPNGGRY
QKEFCMELYFKTPAGQWNDDICTAKHHFICQEKK

LJM11 (SEQ ID NO: 63)
MKVFFSIFTLVLFQGTLGADTQGYKWKQLLYNNVTPGSYNPDNMISTAFAYDAEGEKLFLA
VPRKLPRVPYTLAEVDTKNSLGVKGKHSPLLNKFSGHKTGKELTSIYQPVIDDCRRLWVVDI
GSVEYRSRGAKDYPSHRPAIVAYDLKQPNYPEVVRYYFPTRLVEKPTYFGGFAVDVANPKG
DCSETFVYITNFLRGALFIYDHKKQDSWNVTHPTFKAERPTKFDYGGKEYEFKAGIFGITLGD
RDSEGNRPAYYLAGSAIKVYSVNTKELKQKGGKLNPELLGNRGKYNDAIALAYDPKTKVIF

FAEANTKQVSCWNTQKMPLRMKNTDVVYTSSRFVFGTDISVDSKGGLWFMSNGFPPIRKSE
KFKYDFPRYRLMRIMDTQEAIAGTACDMNA

LJS138 (SEQ ID NO: 65)
MQSKILSFVLFTLSLGYVLGETCSNAKVKGATSYSTTDATIVSQIAFVTEFSLECSNPGSEKISL
FAEVDGKITPVAMIGDTTYQVSWNEEVNKARSGDYSVKLYDEEGYGAVRKAQRSGEENKV
KPLATVVVRHPGTYTGPWFNSEILAAGLIAVVAYFAFSTRSKILS

LJL124 (SEQ ID NO: 67)
MVSILLISLILNLLVFYAKARPLEDISSDLSPDYYITEGYDGVKEKREIELVPVTFGIFNIHTTPA
PRITFEW

LJL35 (SEQ ID NO: 69)
MKLFCLIFVVFVALEVCIETVKAMEATEEISVKLQDDANEPDDSLDLDEGLPDAFDEDYNNQ
AEYKPNPRGDYRRR

In one embodiment, a polypeptide including SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67 is disclosed herein. Homologous polypeptides having an amino acid sequence at least 75%, 80%, 85%, 90%, 95%, 98%, or 99% identical to the amino acid sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67 are disclosed herein. Fusion proteins including SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67 are also disclosed herein.

Fragments and variants of the *Lu. longipalpis* polypeptides identified above are disclosed herein and can readily be prepared by one of skill in the art using molecular techniques. In one embodiment, a fragment of a *Lu. longipalpis* polypeptide includes at least 8, 10, 15, or 20 consecutive amino acids of a *Lu. longipalpis* polypeptide. In another embodiment, a fragment of a *Lu.*

longipalpis polypeptide includes a specific antigenic epitope found on a full-length *Lu. longipalpis* polypeptide.

In one embodiment, a fragment is at least 19 amino acids, at least 23 amino acids, at least 25 amino acids, or at least 30 amino acids in length from any polypeptide (including polypeptides as given in SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67 conservative variants thereof, and homologues thereof), or any fragment that retains at least an epitope.

Fusion proteins including a *Lu. longipalpis* polypeptide can also be produced using methods known to one of skill in the art. In one embodiment, a fusion protein includes an amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, or a conservative variants thereof, and a marker polypeptide. Marker polypeptides include, but are not limited to, polypeptide tags, such as a polypeptide to aid in protein purification (for example, six histidine residues or c-myc polypeptide), or an enzymatic marker (for example, alkaline phosphatase), or a fluorescent maker (for example, green fluorescent protein).

One skilled in the art, given the disclosure herein, can purify a *Lu. longipalpis* polypeptide using standard techniques for protein purification. The substantially pure polypeptide will yield a single major band on a non-reducing polyacrylamide gel. The purity of the *Lu. longipalpis* polypeptide can also be determined by amino-terminal amino acid sequence analysis.

Minor modifications of the *Lu. longipalpis* polypeptide primary amino acid sequences may result in peptides which have substantially equivalent activity as compared to the unmodified counterpart polypeptide described herein. Such modifications may be deliberate, as by site-directed mutagenesis, or may be spontaneous. All of the polypeptides produced by these modifications are included herein.

Polynucleotides encoding salivary polypeptides from *Lu. longipalpis* sand fly are disclosed herein, such as polynucleotides encoding SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67.

Specific, non-limiting examples of *Lu. longipalpis* nucleic acid sequences include SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:16, SEQ ID NO:18, SEQ ID

NO:20, SEQ ID NO:22, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, or SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:68, and degenerate variants thereof. These polynucleotides include DNA, cDNA, and RNA sequences that encode a *Lu. longipalpis* polypeptide. It is understood that all polynucleotides encoding a *Lu. longipalpis* polypeptide are also included herein, as long as they encode a polypeptide with the recognized activity, such as the binding to an antibody that recognizes the polypeptide, the induction of an immune response to the polypeptide, or an effect on survival of *Leishmania* when administered to a subject having leishmaniasis or who undergoes a decrease in a sign or a symptom of *Leishmania* infection.

The polynucleotides of the disclosure include sequences that are degenerate as a result of the genetic code. There are 20 natural amino acids, most of which are specified by more than one codon. Therefore, all degenerate nucleotide sequences are included in the disclosure as long as the amino acid sequence of the *Lu. longipalpis* polypeptide encoded by the nucleotide sequence is functionally unchanged.

Specific, non-limiting examples of a polynucleotide encoding a *P. ariasi* polypeptide are set forth below:

LJL34 (SEQ ID NO:2)

AGTTGTGGAGCTTTTGGTCATTTTACGTGATGTTGCAAATTAAACATCTTCTGATTTTTGT
GGGATTGCTCGTGGTTGTTAATGCACAGAGCAATTACTGCAAACAGGAATCGTGCTCAT
CGGGAGGTGTTGAGAGACCCCATATTGGGTGCAAAAACTCTGGAGATTTTTCCGAAACT
TGCTCCGGAGATGCAGAAATTGTTAAGATGGACAAGAAGAAGCAGAACCTCCTTGTGAA
AATGCACAATCGCCTGAGAGATAGATTTGCTCGTGGTGCAGTGCCAGGTTTTGCACCAG
CTGCGAAAATGCCAATGCTTAAATGGAACGATGAACTGGCCAAATTGGCAGAGTACAAC
GTGAGAACGTGCAAATTTGCCCACGATAAATGCCGCGCAATTGATGTCTGCCCCTATGCT
GGACAGAATCTAGCTCAAATGATGTCCTATCCTACCCATCGAGATCTAAACTATGTTCTT
AAGAATCTCACAAGGGAATGGTTCTGGGAGTACAGATGGGCTAAGCAATCTCAGCTTGA
TAATTACGTGGGTGGTCCTGGGAAAGACAACAAACAAATTGGACATTTCACAGCTTTTG
TGCATGAGAAAACAGACAAAGTTGGATGCGCTATAGCTCGATTTACAAATGAGCACAAT
TTTAAGGAGACCCTCCTAGCTTGCAACTACTGCTACACGAATATGATGAAGGAGAGGAT
CTACACGCAGGGAAAACCTTGTTCACAGTGTCAGAGCAAAAAGTGTGGGCCAGTCTACA
AGAACCTGTGTGATCCTTCGGAGAAGGTTGATCCAACTCCTGATGTCCTTAAGCAATGG
AAGCATGGAAAATGATTATTAAGCTCACTTCAAATGTTTCCAATCCAAAAAAAAAAAAA
AAAAAAAAAAAAAAAA

LJL18 (SEQ ID NO:4)

TTTTGAGAAAAACATTTCCTTGTGAGTTAAATAGTTGGTAAATTAAATCAAGAGAATGTT
GCTTCGTTCCTTGTTTGTTCTTTTTCTAATTTTCTTAACATTCTGCAACGCTGAGGAAGAA

CTTATTGAGAGAAAGTTAACAGGAAAAACGATCTATATCTCAACAATAAAGCTTCCGTG
GTTCCAAGCTCTTAATCATTGTGTTAAAAATGGCTACACAATGGTGTCAATTAAGACATT
TGAAGAGAATAAAGAACTCCTTAAAGAACTCAAAAGGGTGATTAGGACAGAAGATACA
CAAGTTTGGATTGGAGGCCTCAAACATCATCAATTTGCAAACTTTCGTTGGGTAAGCGAT
GGAAGCCACGTAGCAACAGCTTCAGGGTACACCAATTGGGCCCCAGGGGAGCCAGCTG
ATTCCTTCTATTACGATCAATTTTGCATGGCGATGTTGTTCAGAAAAGACGGCGCTCCGT
GGGATGATTTGAATTGTTGGGTTAAGAATCTTTTTGTTTGTGAGAAACGAGATGATTGAG
AGGCTATTTTTGTTATCTCACCGTTTTGTTGAATAAAAAAGAAGAAGAAAGACAAAAAA
AAAAAAAAAAAAAAAAAAAAAA

LJS193 (SEQ ID NO:6)

TACTTCGTACTCTCAGAATTTCTTACAAGTTCCTTTTTCTCTTAACTTTTAAAGTTTTATTT
AACAAAATTGCTCCATTTTTTCGTTTTCTGAATATTCTGTTGAAATTTTGATTAATCTATT
TTATGTGCAGTTTTTACTAAAAATCCCTTATCAGCAACCCGGTGTCTACAGTTTTGTCAC
GCTCAGTAGCATCTTCAAGGTGGTAAGAAAAAATGAAACTCCTGCAAATCATCTTCTCTC
TCTTCCTGGTCTTTTTCCCGACCTCAAATGGGGCCCTGACCGGAAATGAAAGTGCAGCAA
ATGCAGCTCCCTTGCCTGTCGTCCTGTGGCACGGGATGGGCGATTCTTGCTGCTTTCCCTT
CAGTTTGGGAAGCATAAAAAAAATTAATTGAACAACAAATTCCTGGGATTCATGTTGTTA
GCCTGAAAATTGGAAAGTCTCTCATTGAGGACTATGAAAGTGGATTTTTTGTTCATCCAG
ACAAGCAAATTCAGGAAGTTTGTGAGTCACTTCAGAACGATCTAACACTCGCAAATGGA
TTCAATGCAATTGGATTTTCTCAGGGTAGTCAGTTCCTGCGAGGTCTTGTGCAACGATGT
TCTTCTATACAAGTAAGGAATCTCATTTCCATTGGAGGACAGCATCAAGGGGTTTTTGGT
CTGCCCTATTGTCCTTCGTTGAGCAGAAAGACTTGCGAATACTTTAGAAAGCTCCTGAAT
TATGCAGCTTATGAAAAATGGGTACAGAAACTCCTAGTTCAAGCCACCTACTGGCATGA
TCCTCTAAATGAGGATGCATATCGGACTGGAAGCACTTTCCTTGCTGATATAAATAATGA
GAGACAAATCAATAATGACTATATTAATAATATTCGGAAGCTAAATCGTTTTGTGATGGT
AAAGTTCCTCAACGACAGCATGGTTCAGCCAATTGAATCTAGTTTCTTTGGATTCTACGC
TCCAGGAACTGATACAGAAGTTCTCCCATTAAAACAAAGCAAGATTTATTTGGAAGATC
GTTTGGGACTTCAATCAGTACCGATAGATTATCTAGAATGCGGAGGAGATCATTTGCAA
TTTACAAAAGAATGGTTCATAAAGTTTATCATACCCTATCTGAAGCAATAAGAGCTGCA
ATGTAATTGATTAAAAAATGTTAACCATTTCAGGATGATTGGGTGACCCCTTAAAAATAT
AAATGAAAAAATATACAAAAGAAATAAATTTTTATATTGATCCCACAAAAAAAAAAAA
AAAAAAAAAAAAAAAAA

LJS201 (SEQ ID NO: 8)

GGATCGGCCATTATGGCCGGGGCAGTTAATCGCCACAATTTAATAAAATGAGGAACTTT
GCTGTAGTCAGTTTAGCCGTTGCTGTCCTGCTCTTCTGTGCATGGCCTATAAATGCGGAA
GATAATGAAGAAGTTGGAAAGGCGAGAGAAAAAAGAGGCTTAAAAGACGCAATGGAA
CACTTCAAAAATGGATTTAAGGAGCTGACAAAGGACTTTAAACTTCCAAGCCTTCCAAG

TCTTCCTGGATTTGGTAAAAAGCCTGAATCTGGAAGTTCTGAAGATTCTGGAGATAAAA
CTGAGGATACCAGTGGATCTAAGGACGACCAATCAAAGGATAATACGGTCGAAGAATCT
TAAGAAAGGCGCAAATAGCTATTTTCAAAGTGGCGAATGTTTCTTTCTTTATCTGAAATA
AATATTTTTAAACCTTTCGAAACCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

LJL13 (SEQ ID NO:10)

ACTTAAAGATTTTTGTTTAAGCAAAATGAACTTCTTGTTGAAAATTTTCTCTTTGCTCTGT
CTCTGTGGACTGGGGTATTCATGGCAGGATGTGAGAAATGCCGATCAAACCCTCTGGGC
GTATAGATCGTGCCAAAAGAATCCTGAAGATAAGGATCACGTACCTCAATGGAGGAAGT
TCGAATTACCCGACGATGAAAAGACTCATTGCTACGTCAAGTGCGTATGGACGCGTTTG
GGAGCTTACAATGAAAATGAAAATGTTTTCAAAATTGATGTCATTACTAAGCAATTTAAT
GAACGTGGCCTAGAAGTTCCGGCTGGACTTGATCAAGAATTGGGTGGTTCTACAGATGG
AACTTGCAAAGCAGTTTACGATAAATCCATGAAGTTCTTCAAATCTCATTTTATGGACTT
TAGGAATGCTTACTACGCAACTTATGACGGTTCTGATGAATGGTTTAGCAAGAACCCTG
ATGTAAAACCGAAAGGAACAAAAGTTTCCGAATACTGCAAAAATAAAGATGATGGAGA
TTGCAAACATTCCTGCAGTATGTACTACTACCGCTTAATCGATGAAGACAACTTAGTTAT
TCCGTTCAGCAACTTACCTGACTATCCCGAAGATAAGCTCGAGGAATGCAGGAATGAAG
CCAAGTCCGCAAATGAGTGCAAATCATCTGTTATCTATCAGTGTTTGGAAAATGCGGAT
AAGTCAGCTTTAGACGCGTCTTTGAATATACTCGATGAGTTTTCTGGAAGATATTAAAAC
AAACTGGATAAAAAACTTAGGCCAACCTATGATTCGAACTTACGATTTTGAACTTGAAA
TTCATGTGCTTTAACCTATTGTCCCACTAGGAAGAAAAATCCATATTTGGTGATGTTAAA
CTATTTTTGAACCTCTTCAAAATAAACAATTTTCAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAA

LJL23 (SEQ ID NO:12)

AAAGAGAAGTAGTGAGAATGTTTCTTAAGTGGGTTGTTTGTGCTTTTGCGACTGTCTTCC
TTGTTGGGGTGAGTCAGGCAGCCCCACCGGGGGTTGAATGGTATCACTTTGGTCTGATTG
CTGATATGGACAAAAAATCCATCGCGAGTGACAAAACCACCTTTAACAGCGTCCTAAAG
ATCGATGAATTGCGCCACAACACAAAAACGGATCAATACATTTATGTGCGTAGTCGAGT
GAAGAAGCCCGTTTCCACGAGGTATGGGTTCAAAGGACGCGGTGCGGAATTGTCGGAAA
TTGTTGTCTTCAACAATAAACTTTACACAGTTGATGATAAATCTGGAATTACGTTCCGCA
TAACGAAAGACGGAAAACTCTTCCCGTGGGTTATTCTCGCAGATGCCGATGGACAGCGA
CCCGATGGCTTTAAGGGTGAATGGGCTACAATTAAGGATGATACAATCTATGTTGGATC
TACGGGGATGCTCAAGTTCACTTCATCCCTTTGGGTGAAGAAGATCACGAAAGATGGCG
TTGTTACGAGTCACGATTGGACTGATAAATACCGAAAGATTCTCAAAGCTCTAAACATG
CCAAATGGTTTTGTCTGGCATGAGGCTGTTACGTGGTCTCCATTCAGGAAGCAATGGGTC
TTCATGCCGAGAAAGTGCTCAAGGCATCCCTTCTCACAGGAACTCGAAGAACGCACAGG
GTGCAATAAAATAGTGACGGCAGATGAGAATTTCAACGACATTCAAGTTATTCACATTC

AAGATCAGCCATATAATTTAGCTTCTGGTTTCTCTTCCTTCCGCTTTATTCCTGGTACGAA
AAATGAAAGACTTCTCGCCTTGAGGACAGTAGAGCAGGAAGATCAGGTTAAAACTTGGG
CTGTGGTCATGGATATGAAAGGAACAGTTCTGATGTACGAAAAGGAACTTTATGACGAA
AAATTCGAAGGTTTAGCATTCTTTGGTGGTATTAAAAAGAATTAATTTGTTCCAGAAGCT
TTTAGATGAAATAATAAATTTTATTTCATTTTAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AA

LJM10 (SEQ ID NO: 14)
CGCGGCCGCGTCGACCGACAGAAGGGGTAGTTTGTAGAGAACTTTGAGTTCTAAAGGAA
ATTCTCAAGAAGAAAATATTCAAAAGTAAAGAATGGCGTTGAAGTTTCTTCCGGTTCTCC
TTCTAAGCTGCTTCGCAATGAGCACGGCACTACAAGTTACTGAGAAGGAACTTTCTGAT
GGGAAAAAAGATCTTCATCTCCAAAGTTGAGCTAAACTGGTTCGAAGCTCTTGATTTCTGT
ATCCATCGTGGTCTTACGTTGCTCTCAATTAAATCCGCCAAGGAAAATGTAGACGTAACA
AAAGCAATTCGGGCTGAATTGAATTTTGATTCAAAGAAATTGGCTCATGTGTGGACTGG
AGGTATTCGCCATAGTCAAGATAAGTATTTCCGTTGGATAAATGATGGAACTAAAGTTG
TTAAACGAGTCTACACCAATTGGTTCACTGGAGAACCAAATAATGGTTACTGGAAGGAT
GAATTTTGTCTGGAAATTTACTATAAAACCGAAGAAGGGAAGTGGAATGATGATAAATG
TCACGTGAAGCATCATTTTGTATGTCAAGAAAAGAAATAAATTGATTGATTTTGTTTGCT
GATTTGCAGTTCAGAATTGAAAAGCCAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

LJL143 (SEQ ID NO: 16)
CTTCTTTGGATTTATTGAGTGATTAACAGGAAATTAGCTGAAGAAATGAATTCGATTAAT
TTCCTATCAATAGTTGGTTTAATCAGTTTTGGATTCATTGTTGCAGTAAAGTGTGATGGT
GATGAATATTTCATTGGAAAATACAAAGAAAAAGATGAGACACTGTTTTTTGCAAGCTA
CGGCCTAAAGAGGGATCCTTGCCAAATTGTCTTAGGCTACAAATGCTCAAACAATCAAA
CCCACTTTGTGCTTAATTTTAAAACCAATAAGAAATCCTGCATATCAGCAATTAAGCTGA
CTTCTTACCCAAAAATCAATCAAAACTCGGATTTAACTAAAAATCTCTACTGCCAAACTG
GAGGAATAGGAACAGATAACTGCAAACTTGTCTTCAAGAAACGTAAAAGACAAATAGC
AGCTAATATTGAAATCTACGGCATTCCAGCGAAGAAATGTTCCTTCAAGGATCGTTACAT
TGGAGCTGATCCACTCCACGTCGATTCCTATGGGCTTCCGTATCAGTTTGATCAGGAACA
TGGATGGAATGTGGAACGATATAACATTTTCAAAGACACAAGATTTTCCACAGAAGTTT
TCTACCACAAAAATGGTTTATTTAACACCCAAATAACTTATTTGGCTGAAGAAGATTCCT
TCTCTGAAGCTCGAGAGATTACTGCGAAGGATATTAAGAAGAAGTTTTCAATTATTTTGC
CCAATGAAGAGTATAAGAGGATTAGTTTCTTGGACGTTTATTGGTTCCAGGAGACTATGC
GAAAAAAGCCTAAATATCCCTACATTCACTACAATGGAGAATGCAGCAATGAGAATAAA
ACTTGTGAACTTGTCTTTGACACCGATGAACTAATGACCTACGCCCTTGTTAAAGTCTTT
ACTAATCCTGAGAGTGATGGATCTAGGCTCAAAGAAGAGGATTTGGGAAGAGGATAAA
TCTTCTTAATAAAAAAAAGTTCTGTAAGAAAATATTGTTCAATAAATTAAAAAAAAAAA
AAAAAAAAAA

LJS142 (SEQ ID NO: 18)

AATAGATCTTCAAAACGTCTAAGAATGGCTTTCAGCAACACTTTATTTGTTCTTTTTGTG
AGTTTTTTAACGTTTTGTGGCGCTGATCAGACACTTATTGAGAAGGAATTAACCGGAAGA
ACTGTTTATATCTCCAAAATTAAGCTAAATTGGAACGATGCCTTCGATTACTGCATCCGC
AATGGCCTCACCTTTGCTAAGATTAAATCAGCTGAAGAAAACACCGAACTGAGTGAGAA
ACTCAAGACAGTCATTCGTACGGAGGAGTTTCAAGTTTGGATTGGAGGCATTGAACATC
ATCAAGACAGTTCCTTCCGCTGGGTAAGCGACTCCCAACCAATAACCAACAAATTGGGC
TACAAATACACAAACTGGAATACCGGAGAGCCCACAAATTACCAAAACAACGAATATT
GCTTGGAAATATTATTCCGGAAGGAAGATGGAAAATGGAATGATTTTCCCTGCAGTGCA
AGACATCATTTTGTTTGTGAAAAAAGAACAAAATAAAATGAAGAAAATGTGATTTTCCT
TTGGTTGAAGAATAAAATTCTGTTGAAAAAAAAAAAAAAAAAAAAAAAAAAAA

LJL17 (SEQ ID NO: 20)

ATTTAGTTTGTGTTTAACAAAACAAGAATGCAGAACTTCCTTTTAGTTTCCTTGGCTTTAG
CTGCCTTAATGCTATGTGCCGAAGCAAAGCCGTACGATTTTCCGCTTTATCAGGACTTAA
TTCAGGGCGTTATTCAGCGCGAAAGTCAAGCTGAGAGGGAGAAGAGAAGCCCCAATGA
GGACTATGAGAAGCAATTTGGGGATATTGTTGATCAAATTAAGGAAATTAGTTTCAATG
TCATGAAAATGCCCCATTTTGGAAGCTCTGATGATAATCGTGATGATGGCGAGTACGTTG
ATCATCATTATGGTGACGAAGATGATCGTGATTATGATCATTACTAAATACTACTTGCTC
CTGCTGAATGACTTGAAGGAATCATTTTTTTGCAAAAATATCCATCAAATTATTGAATTA
ATAAAGTTGCAAAAAAAAAAAAAAAAAAAAAAAAAAAA

LJM06 (SEQ ID NO: 22)

GTTTAAGGAATTTCTTTCATCTCAGTCTTCGATTTTCTTTAAACAAATAATGAAGTTTTAT
ATTTTTGGAGTTTTCCTGGTGAGCTTTCTTGCATTATGCAATGCTGAGGATTATGATAAA
GTAAAACTTACTGGAAGAACTGTTTACATCTCCAGATCAAAGGCTCCGTGGTTCACAGCT
TTAGACAATTGTAATCGTTTACGCTTCACCTTCGCCATGATCAAGTCTCAGAAGGAGAAT
GAAGAGCTAACAAATGCGCTTTTAAGTGTAATTAAATCTGACGAAGAAAATGTTTGGAT
TGGAGGTCTTAGGCACGATCTGGATGACTACTTCCGTTGGATTAGTTTTGGAACTGCATT
GTCAAAGACTTCGTACACCAATTGGGCCCCAAAGGAACCC
ACAGGAAGGCCCCATAGAACTCAAAATGATGAATTCTGCATGCAAATGTCTTTCAAAGA
TGGTGGCAAATGGAGTGATAACACCTGTTGGCGTAAACGTTTGTACGTTTGTGAAAAGC
GTGATTAAATAAAGGAACACTGCCAATGAATATTGGGCAATTTGAGAGAAATTAAATTA
AAAAAAAAAAAAAAAAAAA

LJM17 (SEQ ID NO: 24)

AGTCAGTGTTAATGAAGAAATTGCAATTATGAGGTTCTTCTTTGTTTTCCTTGCCATCGTC
CTTTTTCAAGGGATCCACGGAGCTTATGTGGAAATAGGATATTCTCTGAGAAATATTACA

TTCGATGGATTGGATACAGATGACTACAATCCAAAGTTCAACATTCCAACGGGTTTGGC
AGTTGATCCCGAAGGATATAGGCTCTTCATAGCCATCCCAAGGAGAAAGCCAAAGGTTC
CCTACACTGTGGCTGAACTGAATATGGTCATGAATCCCGGATTTCCCGTCGAGAGAGCTC
CGAGCTTTGAGAAATTCAAAAAATTCAATGGCGAGGGCAAAAAGGATCTTGTTAATGTG
TATCAGCCAGTCATTGATGATTGTCGTCGTCTTTGGGTGCTTGACATTGGGAAGGTGGAA
TACACCGGTGGTGATGCTGATCAATATCCCAAAGGAAAGCCTACCCTAATTGCCTACGA
CCTCAAGAAGGATCATACTCCGGAAATTCATCGATTTGAAATTCCAGACGATCTCTATAG
CTCACAAGTTGAATTTGGTGGATTTGCCGTTGATGTTGTTAACACGAAAGGAGACTGTAC
GGAGTCATTTGTCTACCTGACCAATTTCAAGGATAACTCTCTAATTGTCTACGATGAGAC
ACAAAAGAAAGCTTGGAAATTCACAGATAAAACATTTGAAGCTGATAAGGAATCCACGT
TCTCCTACTCGGGAGAGGAACAAATGAAGTACAAAGTCGGTCTTTTTGGGATAGCTCTG
GGTGATAGGGATGAAATGGGGCATCGTCCTGCCTGCTACATCGCTGGGAGTAGCACCAA
AGTCTACAGTGTTAACACTAAAGAACTCAAAACAGAGAATGGTCAGTTAAATCCTCAGC
TTCACGGTGATCGTGGAAAGTACACAGATGCAATTGCCCTAGCCTACGATCCTGAGCAT
AAAGTCCTCTACTTTGCTGAATCCGACAGCAGGCAGGTGTCCTGTTGGAATGTAAATATG
GAGCTAAAACCAGACAATACGGATGTGATCTTCTCTAGTGCCCGTTTTACTTTTGGAACG
GATATTTTGGTTGATAGCAAGGGAATGCTGTGGATAATGGCTAATGGACATCCACCAGT
AGAGGATCAAGAGAAGATTTGGAAGATGAGATTCGTAAACCGGAAGATCCGTATTATG
AAAGTGGATACGGAACGTGTTTTCAAATATTCACGCTGCAATCCAAATTATAAGCCCCC
AAAGGAAATTGAAGTTTGAGACACAGGAAAAAGCTCAATTTTCAACAAGAATTTGATCT
TAATCTGAATACCCTAAAGTCTGTCAAAGAATTTCATATTATTTGAAAACCAATAAATTG
ATTAATTTTCCGAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

LJL04 (SEQ ID NO: 26)

ACTAAAGCGTCTCACCGAAATCAGGGAAAATGATTAAGGAAGTTTTCTCTCTGGCTCTA
CTTGTGGCCTTGGCACAGTGTGCTAATGAAATCCCTATTAATCGTCAGGGGAAAGATTAT
CCAGTTCCGATCATTGATCCAAATAAATCATCTTCGGATGATTATTTCGATGATCGCTTC
TACCCTGATATTGATGATGAGGGCATAGCTGAGGCTCCTAAGGATAATAGGGGAAAATC
CCGTGGTGGTGGTGCGGCTGGCGCAAGAGAAGGTAGGTTAGGTACGAATGGGGCTAAA
CCGGGTCAGGGTGGAACTAGACCAGGACAGGGTGGAACTAGGCCAGGACAGGGTGGAA
CTAGGCCAGGTCAGGGTGGAACTAGGCCAGGTCAGGGTGGAACTAGACCTGGGCAAGG
TAGAACTAAGCCTGCTCAGGGAACTACTAGGCCAGCTCAGGGAACTAGAAATCCAGGAT
CGGTTGGTACGAAAGAAGCCCAGGATGCGTCAAAACAAGGTCAAGGTAAAAGAAGGCC
AGGGCAAGTTGGTGGTAAAAGACCAGGACAAGCAAATGCTCCTAATGCAGGCACTAGA
AAGCAACAGAAAGGCAGTAGAGGCGTTGGAAGGCCTGATCTATCGCGCTACAAAGATG
CCCCTGCTAAATTCGTTTTCAAATCTCCCGATTTCAGTGGAGAAGGCAAAACTCCAACTG
TAAATTACTTTAGAACGAAGAAGAAGGAGCACATTGTGACCCGTGGTAGTCCTAATGAT
GAATTTGTTCTGGAGATTCTCGATGGGGATCCAACTGGGCTTGGACTAAAGAGTGAAAC
CATAGGCAAAGATACGCGTTTAGTGCTGGAGAATCCTAATGGAAATTCCATCGTGGCTC

GTGTTAAGATCTACAAGAACGGTTATTCAGGATGAAGAAGAAATCCTTTGATTTCCCCCC
CCCCCTCTTCCTTTAAAATTCAACATAATAAAAAAAAAAAAAAAAAA

LJM114 (SEQ ID NO: 28)

GTCTTTTCCTGAGTGTTTCATTAACAAAATGAATTCAGTAAACACTTTAATTTTAACTCTT
CTATTTGCAATTTTTTTATTAGTGAAAAGGTCTCAGGCTTTTCTTCCATCTGACCCAAGTA
TCTGTGTTAAAAATTTAGTATTGGATACAGGAAGGACTTGTGAGGAAAGTGAATATTTTC
CGGATATCAAGAACGTTAAAAATGGAAAAAGAGTTTACATTGTCTGCACTGATTCAGAT
GCAGTTGATTATAAATTTTATATTTGTTTCGATATGAATCGTCTTTCTGGACCACCGTATC
CTGAGGAAGAAATCCTTCGTGAATCAACGGTAACTTATGCCCAAATTTATGAGCTGATG
ACTACGGAAACCACTGAAACCAAAAAGCCAAAAAAGAAACCAAAGAATTCAAAAACGG
ACCCAGACCCTCCAGCAATTCGTCCAGGATTTTCATTTAGAAATTCAATTTCTGTTTAATT
TTACAATTTATTTTGAAAGAAAAATGATATTTCGAAATATTCTATACAAAAAAACAACA
GTTATAAAACGAAAATTCAATCATTTCAATGAGAAAACTTAGTCTTGAGTAAGGTTTATT
CACCACCCGACGCCACGCTATGGTGAATAATTTTCTTTATTCACCACATCAAAATGACGG
CTTATAAACTTCAACAAATAGTTTGGAAAATACATTTCTAACTAATGCAATGTTTACTTA
AAATCACTTTACAAATTCACGCATTTGAGATGCAACAAATATATACAATTCAACGATAT
AAACTTTCCACAAGGAAAACTTTCAACCAAAAAAAAAAAAAAAAAAAA

LJM111 (SEQ ID NO: 30)

ATCATTCAAAAGGCAGCAGCACAATGAAGTTATTTTTCTTTCTTTACACTTTTGGTCTAGT
CCAAACGATTTTTGGAGTAGAAATTAAACAAGGATTTAAATGGAATAAAATCCTTTATG
AGGGCGATACATCAGAAAACTTCAATCCAGATAACAACATCCTTACGGCTTTTGCGTAC
GATCCTGAGAGTCAGAAACTCTTCCTAACTGTCCCGAGGAAATATCCCGAAACTATGTA
CACTTTGGCAGAAGTTGATACTGAGAAAAATTCTTTTGAATCGGGAGATACTTCCCCGCT
CCTTGGAAAATTCAGTGGTCATGAAACTGGGAAAGAACTTACATCAGTTTATCAGCCAG
TTATCGATGAATGTCATCGTCTTTGGGTTGTTGATGTTGGATCAGTAGAACGTAACTCAG
ACGGCACAGAAGGTCAGCCAGAACATAATCCTACCCTTGTGGCGTACGATCTCAAAGAA
GCCAACTATCCTGAAGTTATTCGTTACACGTTTCCCGATAATTCCATTGAGAAGCCCACA
TTTCTGGGTGGATTTGCCGTTGATGTTGTAAAGCCGGATGAATGCAGTGAAACTTTTGTC
TACATCACAAACTTCCTCACCAACGCCCTCATAGTATACGATCATAAGAATAAGGACTC
CTGGACGGTACAAGATTCAACTTTTGGACCAGATAAAAAGTCAAAGTTTGACCACGATG
GACAACAGTATGAATACGAAGCAGGAATCTTCGGGATTACCCTTGGAGAGAGAGATAA
CGAAGGAAATCGTCAAGCGTACTATTTAGTAGCAAGTAGTACCAAACTTCACAGCATCA
ACACCAAAGAACTGAAGCAAAAAGGAAGCAAAGTTAATGCAAATTATTTGGGAGATCG
TGGTGAATCCACCGATGCCATAGGCTTAGTTTACGATCCAAAAACCAAAACTATCTTCTT
CGTTGAGTCAAATAGCAAAAGAGTATCATGCTGGAATACCCAGGAAACACTAAACAAG
GATAAAATTGATGTAATCTATCACAATGCAGACTTTTCCTTTGGAACAGATATATCGATT
GATAGTCAGGATAATTTGTGGTTCCTAGCAAATGGACTTCCACCTCTGGAAAATTCTGAT

AAATTTGTCTTTACAAAGCCACGTTATCAAATATTCAAAGTCAACATTCAAGAAGCAATT
GCTGGAACTAAATGTGAAAAGAATCTTTAACAAATGAAACTTTGTAGAAAAATACATAA
TATCTGAATAAAAAGTCATAAATGTACCATAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAA

LJM78 (SEQ ID NO: 32)
CTTTAAAGCAAAAATTTTGTGGGAAAGGAAGTTACCCGGAGATGACGTTTCTAATTATA
CTTGGTGCATTTCTCCTTGTTCAAATTATTACAGCTTCAGCTTTAGGATTGCCTGAACAGT
TTAAAGGTTTAGAGGATTTACCTAAAAAACCTTTGGCAGAGACTTATTATCACGAAGGA
TTGAATGATGGAAAAACGGATGAAATGGTGGATATTTTTAAAAGTCTTAGCGATGAATT
TAAATTCAGTGATGAAAATTTAGATGTTGGTGAGGAGAAAAATTACAAGAAACGTGATA
TAACCCAAAATTCAGTGGCAAGGAACTTCCTATCAAACGTAAAGGGAATTCCTTCAATG
CCATCACTCCCTTCAATGCCTTCAATGCCATCAATTCCTTCACTTTGGTCAAGTCAGACA
CAGGCGGCACCAAATACCGCACTTGCCCTTCCTGAATCTGATTATTCCCTTCTAGATATG
CCGAATATTGTGAAAAATTTCCTAAAGGAAACAAGAGACCTCTATAACGATGTTGGAGC
TTTTCTTAAGGCAATTACAGAAGCTTTAACAAATAGATCTTCATCATCTCAACTTCTTTCC
TCCCCAATGGTGAGCACGAATAAAACCAAAGAATTTATTCGGAATGAAATACAAAAAGT
CCGAAAAGTGAGAAATTTCGTCCAGGAAACTCTTCAGAAAATCCGAGACATTTCTGCTG
CTATTGCCAAAAAGGTAAAATCATCAGAATGTCTGTCCAATCTTACGGACATCAAAGGA
CTTGTATCAGACGGAATTAATTGTTTAAAGGAAAAATTCAATGATGGAAAACGAATTAT
CCTGCAATTGTACAATAATTTACTAAAAGGACTCAAAATTCCAAATGACCTAATGGTTG
AATTGAAGAAATGTGATACAAATCAAAACAATACTTTGGGAAGAATAATCTGTTATTTT
TTGACACCATTGCAACTGGAAAAAGAACAAATTCTTCTACCTGTAGAATTTATAAAGCG
CATTCTTGAATTAACCCACTACTTTTCCACAATGAAAGAAGATCTTATCAACTGTGGCAT
CACAACGATTGCATCCATTACGTAAAAAATGGAAAAATGTGCCGGTGAAATGCTTGAAA
TCACCAAAGAAATTTCATCGCAAATAACAGTTCCAGAATAACCAAATTTTAATGATTACT
TCTCAAGGAAAATACTACCAAAAGGCATTAATTAAAACGATGTTTTTTATAAACAATGT
AAGAAAAAAAAAAAAAAAAAAAAAAAA

LJS238 (SEQ ID NO: 34)
AGTTAATCTTCTGTCAAGCTACAAAAATGCTTAAAATCGTTTTATTTCTATCAGTTTTGGC
TGTATTAGTGATTTGTGTAGCAGCAATGCCAGGATCCAATGTTCCTTGGCACATTTCACG
AGAAGAGCTTGAGAAGCTTCGTGAAGCTCGAAAGAATCACAAGGCACTCGAGAAGGCA
ATTGATGAATTAATTGACAAATATCTCTGATTTTGAAGAGCAAGGAAGAGGAAATAAAC
GGCCGAGGAAGGATTTTCTTTAGAGATTCTTCTTTTTATTACTTCAAACCTAACTTCAAA
ATCAGTCTGATATTTTTTTAATTTGAAAAAAATATTGAAAATTTTAACTATTTGTGAAATT
TAAATAAATAAAGAATGTCAGAAGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

LJS169 (SEQ ID NO: 36)

AATTTTCACCATGAAGTTTTCTTGCCCAGTTTTCGTTGCAATTTTCCTTTTGTGCGGATTTT
ATCGTGTTGAGGGGTCATCACAATGTGAAGAAGATTTAAAAGAAGAAGCTGAAGCTTTC
TTTAAGGATTGCAATGAAGCAAAAGCCAATCCTGGTGAATACGAGAATCTCACCAAAGA
AGAAATGTTTGAAGAATTGAAAGAATATGGAGTTGCTGACACAGACATGGAGACAGTTT
ACAAACTTGTGGAAGAATGTTGGAATGAATTAACAACAACGGATTGTAAGAGATTTCTC
GAAGAGGCTGAATGCTTCAAGAAGAAGAATATTTGTAAATATTTCCCAGATGAAGTGAA
ATTGAAGAAGAAATAAATTTTTAGCTTGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAA

LJL11 (SEQ ID NO: 38)

AGTTGCAAGAATTTCTTCATTGCGTTAAGATGTTGTTTTTCCTTAACTTTTTTGTGCTGGT
GTTCAGCATAGAACTGGCGTTGTTAACAGCATCAGCAGCAGCAGAAGACGGCAGCTATG
AGATCATAATTCTTCACACCAATGATATGCACGCGCGTTTTGATCAAACCAATGCTGGAA
GCAACAAATGCCAAGAAAAAGACAAGATTGCTTCCAAATGCTACGGAGGATTTGCAAG
AGTTTCAACAATGGTGAAAAAATTCCGAGAAGAAAATGGCAGCAGTGTCTTGTTCTTGA
ATGCTGGTGACACGTATACAGGTACCCCATGGTTTACCCTCTACAAGGAGACCATTGCA
ACGGAGATGATGAACATCCTTCGTCCAGATGCAGCCTCACTGGGAAATCATGAATTCGA
CAAAGGAGTAGAAGGACTCGTGCCATTCCTCAATGGTGTCACCTTCCCTATTTTAACAGC
GAATTTGGACACTTCTCAAGAGCCAACAATGACCAATGCTAAAAATCTCAAACGCTCAA
TGATTTTTACGGTTTCCGGGCACAGAGTTGGTGTAATTGGCTACCTAACGCCTGATACAA
AATTCCTCTCGGACGTTGGTAAAGTTAATTTTATTCCGGAAGTTGAAGCCATCAATACGG
AAGCACAGCGTCTGAAGAAAGAGGAAAATGCCGAAATAATCATCGTTGTTGGACATTCA
GGGTTGATAAAAGATCGAGAAATTGCAGAGAAATGCCCACTGGTTGACATAATTGTTGG
AGGACATTCACACACATTCCTCTACACAGGAAGTCAGCCTGATCGTGAGGTTCCTGTAG
ACGTTTATCCTGTTGTTGTGACCCAATCCAGTGGGAAGAAAGTTCCAATTGTTCAAGCCT
ATTGCTTTACAAAGTATTTGGGGTACTTTAAAGTGACGATCAACGGAAAAGGAAATGTT
GTGGGATGGACTGGGCAGCCAATTCTCCTTAATAACAACATTCCCCAAGATCAGGAAGT
TCTCACTGCTCTTGAAAAGTACAGAGAACGCGTGGAAAACTATGGAAATCGCGTAATTG
GAGTTTCCCGTGTAATTCTCAATGGGGGGCATACTGAATGTCGTTTCCATGAATGCAATA
TGGGTAATCTCATCACGGACGCTTTTGTGTATGCCAATGTAATCAGTACACCAATGAGTA
CGAATGCCTGGACAGATGCAAGTGTTGTTCTGTATCAAAGTGGTGGCATTCGTGCCCCA
ATTGATCCTCGTACCGCGGCAGGGAGCATCACACGCCTCGAGTTGGACAATGTTCTACC
ATTTGGGAATGCACTGTACGTCGTAAAAGTTCCTGGGAATGTCTTACGCAAAGCTTTGGA
ACATTCAGTTCATCGATACTCCAACACTTCGGGATGGGGAGAATTTCCACAAGTTTCGGG
GCTAAAGATTCGTTTTAACGTCAATGAAGAAATTGGAAAACGCGTAAAGTCCGTTAAAG
TTCTCTGTAGCAATTGCTCTCAACCTGAATACCAACCACTGAGAAATAAAAAAACTTAC
AACGTTATCATGGACAGTTTTATGAAGGATGGAGGTGATGGGTATAGCATGTTCAAGCC

CTTGAAGATCATCAAGACCCTCCCACTGGGAGATATTGAAACAGTAGAAGCTTATATTG
AGAAAATGGGCCCCATTT
TCCCAGCAGTCGAGGGAAGGATCACTGTTCTTGGGGGACTTCAAAAATCAGATGAGGAT
TGGCATTAGAAACATCCTGGACGTTATGGAAAGAATAAAAGAAGGATCATAGAAAAAA
AAAAAAAAAAAATAAAAAAAAAAAAAAAAAAAAAAAAAAAA

LJL08 (SEQ ID NO: 40)
GTCAGTGATCTGATAAGTTATTAAAATGAAGCAAATCCTTCTAATCTCTTTGGTGGTGAT
TCTTGCCGTGCTTGCCTTCAATGTTGCTGAGGGCTGTGATGCAACATGCCAATTTCGCAA
AGCCATAGAAGACTGCAAGAAGAAGGCGGATAATAGCGATGTTTTGCAGACTTCTGTAC
AAACAACTGCAACATTCACATCAATGGATACATCCCAACTACCTGGAAATAATGTCTTC
AAAGCATGCATGAAGGAGAAGGCTAAGGAATTTAGGGCAGGAAAGTAAGAGATTGAGG
AAAATTGTAGCCGAAGAGAGAAGGAAGGAAAGTCCCATATTTTGTTTGTTAATTGTAAC
GAATTTTGCGAAAAAAAATAAAATATTATGCACTCCAAAAAAAAAAAAAAAAAAAAAAA
AAAAAA

LJS105 (SEQ ID NO: 42)
TATTTTTAATAATTCTGTGTAAAATGAACGTTCTTTTCGTGTCTTTCACGCTCACAATTCT
TCTTCTCTGTGTTAAGGCACGGCCAGAAGATTTCGTAGCTCTTCAGGATCAAGCTAATTT
CCAGAAATGCCTCGAACAATATCCAGAACCAAATCAATCTGGAGAAGTTCTTGCGTGCC
TCAAGAAGCGCGAAGGTGCCAAAGATTTCCGGGAAAAGAGGAGCCTGGATGACATAGA
AGGGACTTTCCAAGAGTCTGGAAATCTCTGGGGTGCATAGGAAGCTCAGAGGACTTCTA
ATCAATCTGTGAGAAGAGAACCCAACGGCTAGAGAAAATTTAAGGAAAATAAAGAAAT
TAATGAAGCATTAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAA

LJL09 (SEQ ID NO: 44)
GTATATCAAGTATCATTCAAGTGAATCATTGGCTCCGTAATTTGTACAAAAGAAAAAAA
AAGTTGATAAAATCATGAAAATCACTGTGATTTTATTCACGGGATTTACAATTGCCCTCG
TGAGTAGTGCTGTGCTTAAGAAAAACGGTGAAACTATTGAAGAAGAAGAAGTAAGAGC
TGAGCAACGACTTAGAGAGATCAATGAGGAACTTGATCGTAGGAAGAATATCAATACTG
TAGCCGCTTGGGCTTATGCATCCAATATTACTGAGGTCAATCTCAAGAACATGAATGATG
TGTCGGTTGAAACCGCGAAATACTACAAGGAACTTGCATCTGAATTGAAGGGATTCAAT
GCCAAGGAATACAAGAGTGAGGATCTGAAGAGACAAATTAAGAAGCTAAGCAAGTTGG
GATATAGTGCTTTACCATCTGAGAAGTATAAGGAGCTTTTGGAAGCTATCACATGGATG
GAATCGAATTATGCAAAAGTGAAAGTTTGCTCATACAAGGATCCAAAGAAATGTGATTT
AGCACTTGAACCTGAAATTACGGAAATCCTTATTAAAAGTCGAGATCCTGAGGAACTTA
AATATTATTGGAAACAATGGTACGACAAAGCTGGCACACCAACTCGAGAGAGTTTTAAT
AAGTATGTACAACTAAATCGTGAAGCAGCGAAATTGGATGGATTTTATTCGGGTGCAGA

ATCTTGGCTTGATGAATATGAAGATGAGACATTTGAGAAACAACTTGAGGATATCTTCG
CCCAAATTCGCCCACTGTACGAGCAACTCCATGCTTATGTTAGATTCAAGCTGAGGGAA
AAGTATGGAAATGACGTTGTTTCGGAGAAAGGTCCCATTCCAATGCATCTCTTGGGGAA
CATGTGGGGTCAAACGTGGAGTGAAGTTGCCCCAATTTTAGTCCCATACCCCGAAAAGA
AGCTCCTCGATGTTACCGATGAGATGGTTAAGCAGGGATACACACCAATTTCTATGTTTG
AAAAAGGAGACGAATTTTTCCAAAGCTTGAATATGACGAAACTTCCAAAAACCTTCTGG
GAGTACAGTATTTTGGAAAAACCCCAAGATGGTAGGGAATTGATCTGCCATGCAAGTGC
ATGGGACTTCTATACAAAGGATGATGTAAGGATTAAACAGTGTACCAGAGTTACAATGG
ATCAATTCTTCACGGCTCATCATGAGCTTGGTCACATTCAATATTATTTGCAATATCAAC
ATTTGCCGAGTGTTTACAGAGAAGGTGCCAATCCAGGCTTTCACGAGGCTGTTGGGGAT
GTTCTCTCTCTTTCGGTATCAAGTCCTAAACATTTGGAAAAAGTTGGTTTGCTTAAAGAC
TTCAAATTTGATGAAGAATCCCAGATAAATCAACTTCTAAATTTAGCTCTGGATAAAATG
GCATTCCTCCCATTTGCCTATACCATTGATAAATATCGCTGGGGTGTGTTTCGGGGTGAA
ATTTCGCCGTCTGAGTACAATTGCAAATTTTGGGAAATGCGTTCCTACTATGGTGGTATA
GAACCACCAATTGCACGTTCTGAGAGTGATTTTGATCCACCAGCAAAATATCATATTTCA
TCGGATGTTGAGTACCTCAGGTATTTGGTTTCCTTCATTATTCAGTTCCAATTCCATCAAG
CTGTGTGCCAAAAGACTGGTCAGTTCGTACCGAATGATCCGGAGAAGACTCTTCTAAAT
TGTGACATCTACCAGAGTGCTGAGGCTGGTAATGCCTTCAAAGAAATGCTCAAATTGGG
ATCCTCAAAACCATGGCCAGATGCAATGGAAATTCTTACGGGGCAAAGGAAAATGGATG
CTTCTGCATTAATTGAGTACTTCCGTCCACTCAGTGAGTGGTTGCAGAAGAAGAATAAG
GAACTAGGAGCTTATGTTGGCTGGGACAAATCTACTAAGTGTGTCAAAAACGTCAGTTA
ATTTTTTGTGAGCCCTAAAAAATATTCATAACATTTCAATATGACAAAATATATGATTTT
CGTGAAAACTAAGCATGAGTAAGTTTTTTTTGTGAATTTTTAGCAGTTTCATTTCAGAAT
AAACGTCAAATTTTTAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

LJL38 (SEQ ID NO: 46)

TCAGTTAGTTGACTAACAAACCACAATAGAGACACTAAAATGAAGACATTCGCCTTAAT
CTTCTTGGCTCTTGCTGTTTTTGTGCTCTGCATTGACGGAGCTCCAACTTTTGTGAATTTA
CTGGACGACGTACAGGAAGAGGTAGAAGTTAATACGTATGAGCCTTAGGAAGAAAATG
TTTGAGGAGTTTCAGGCAGAGGCAGAGCTTTCCCAGAGAGGGAGCTTTTGCCTTGCTGT
AGATTTTTAAAAATGAATCAATTTGATTGGAGCAATTACGCTATATTTGTGGGAATATTT
TTGAATTAAAAACTAATTATGGAAATTAATATATAATTTTCAGAATTTCAATAAATTCAT
CAAAATTGTATTAATTAAAAAATATTGTATGAAATTCCCAATAAAAGCTTTCAAATTAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

LJM04 (SEQ ID NO: 48)

GGCCATTATGGCCGGGGATAGAACTTAATTGTTGTTAAAATGAATCACTTGTGCTTTATT
ATTATTGCTCTATTCTTTTTGGTTCAACAATCTTTGGCTGAACATCCAGAAGAAAAATGT
ATTAGAGAATTGGCGAGAACTGATGAAAACTGCATTCTTCATTGTACGTATTCGTACTAC

GGATTCGTTGATAAAAATTTCAGGATCGCTAAAAAACATGTTCAAAAATTCAAAAAAAT
CCTAGTTACATTCGGCGCTGTTCCTAAGAAAGAAAAAAAGAAACTTTTAGAGCACATTG
AGGCTTGTGCGGATTCTGCGAATGCTGATCAACCTCAAACTAAAGATGAAAAATGTACA
AAAATAAATAAGTACTATCGTTGTGTTGTGGATGGAAAAATATTACCCTGGAATAGTTA
TGCTGATGCAATCATTAAGTTTGATAAAACCCTTAACGTATGAAGCAAAGATATTCGAA
AAAAAAACATCAAGATTATGCTGGAAAGAAAAAAATAAAAAAAAAATTGTGCTAATCAA
ATTGAATTAACGCTTAATGCTATATTAAAAAAAAAAAAAAAAAAAA

LJM26 (SEQ ID NO: 50)

GTCGGAGATCGTCTGCCTTGATGATCACATCGTGATTGTGAGTTACAAGAGTGAAACTTT
TTAAGTGTGTGTGTCTTAGCAAAGTGATTTCCACAATGAAGATTATTTTTTTAGCCGCTTT
TCTACTAGCGGATGGTATTTGGGCTGCTGAAGAACCTTCAGTGGAAATTGTAACACCAC
AATCAGTGCGGAGACACGCTACGCCAAAAGCCCAGGACGCGAGGGTAGGAAGTGAATC
CGCAACAACAGCACCAAGACCAAGTGAATCAATGGATTACTGGGAGAATGATGATTTCG
TCCCATTTGAGGGTCCATTCAAGGATATTGGAGAATTCGACTGGAACCTTTCGAAGATCG
TTTTTGAGGAAAACAAAGGTAATGCCATCTTGTCGCCACTCTCTGTGAAGCTACTAATGA
GTTTGCTCTTCGAGGCCAGTGCGTCAGGTACCTTGACCCAGCACCAACTCAGACAAGCC
ACTCCCACCATCGTCACCCACTATCAGTCTCGAGAATTTTACAAGAATATCTTTGACGGT
CTCAAGAAAAAGAGTAACGACTACACGGTTCACTTTGGTACGAGAATCTACGTGGATCA
GTTTGTGACGCCTCGCCAGAGATATGCTGCCATTTTGGAGAAGCATTATCTGACTGATCT
CAAAGTTGAGGACTTCTCGAAGGCAAAAGAAACAACTCAGGCAATCAATAGTTGGGTGT
CAAACATCACAAATGAGCACATAAAGGATCTCGTGAAGGAGGAAGATGTTCAGAATTC
AGTTATGCTCATGCTTAATGCAGTCTACTTCCGCGGACTCTGGCGCAAGCCTTTCAATCG
TACACTCCCACTGCCCTTCCACGTGAGCGCTGATGAGTCCAAGACGACTGATTTTATGCT
AACCGATGGGCTCTACTACTTCTACGAGGCAAAGGAATTGGATGCTAAGATCCTCAGAA
TTCCTTACAAAGGTAAACAATACGCAATGACTGTGATCTTACCAAATTCCAAGAGTGGC
ATTGATAGCTTTGTGCGTCAGATTAACACGGTCCTCCTGCACAGGATTAAGTGGTTGATG
GATGAAGTGGAGTGCAGGGTTATTCTACCCAAGTTCCACTTTGACATGACGAATGAGCT
GAAGGAATCGCTCGTAAAGTTGGGCATCAGTCAGATTTTCACATCAGAGGCATCTTTGC
CATCATTAGCACGAGGACAGGGCGTACAGAATCGTCTGCAGGTGTCTAATGTGATTCAG
AAGGCGGGAATAATTGTGGATGAGAAGGGCAGCACAGCCTATGCTGCGTCAGAAGTGA
GCCTAGTCAACAAGTTTGGAGATGATGAGTTCGTCATGTTCAACGCTAATCATCCATTCC
TCTTTACAATTGAGGACGAAACCACCGGCGCAATCCTATTTACGGGAAAAGTCGTCGAT
CCCACGCAATAGGGAATGAAAAGCATTTCATCGTATACAACTTTTTTTTTAATTAATTAT
TCCTCATTGAAGGACATTAATAGAGCATCTTCTCAGGAAGGCACTCCTGACTTATTTTTA
CTAAATGTGATCCTTGGACACATAAAAAAAACAGCTGTACTTTCTACTTTTTATAATATA
CGACCATATTTGTGAGGAAAAAAAAAAAAAAAAAAAAAAAAAAAA

LJS03 (SEQ ID NO: 52)

TCAGTTAAGCAGATTTTCAAGCTAAAGAAACTTAACTAAGATGCGATTCCTTCTTTTGGC
CTTCTCCGTTGCTTTGGTGCTTTCACCAACATTCGCCAAACCAGGTCTTTGGGACATTGTA
ACTGGTATTAATGATATGGTAAAAAATACTGCGAATGCACTCAAAAATCGTCTAACAAC
TTCTGTGACATTATTCACAAATACCATCACCGAAGCTATAAAAAATGCAAATTCTTCTGT
TTCGGAACTCCTTCAGCAAGTCAATGAAACCCTTACGGATATTATTAATGGTGTAGGACA
AGTGCAGAGTGCCTTTGTGAATTCAGCTGGAAATGTTGTTGTGCAAATTGTTGATGCCGC
TGGAAATGTTTTGGAAGTTGTTGTTGATGAGGCTGGAAATATCGTGGAGGTAGCTGGAA
CAGCATTGGAAACTATCATTCCACTGCCCGGTGTAGTGATTCAGAAGATAATTGATGCTC
TCCAAGGAAATGCAGGGACTACATCGGATTCAGCTTCATCAACTGTGCCCCAACAATCT
TAACTACAACCGCAATGATGTTGTCTTTAACGGAGAATTTTTAAATTTGAATATCAAAAT
CCAAGATGAAATATTCAGATTTTTCAATCAATATGATACGAAATTTTGAAATTATTTTTC
CGACTAAAGCAATTTGTAAAAGGAAAACCAAATAAATATTTGAAATTGTAAAGAAAAA
AAAAAAAAAAAAAAAAAAAAAAA

LJS192 (SEQ ID NO: 54)

ATATCAATTTTATCATCATGGTGAAGTACTCGTGTCTTGTTCTTGTTGCAATTTTTCTTCT
GGCCGGACCCTACGGCGTTGTAGGTTCTTGTGAGAATGACCTGACAGAGGCCGCCAAGT
ATCTTCAAGATGAATGCAATGCAGGTGAAATTGCAGATGAATTTCTACCCTTCTCTGAAG
AAGAAGTGGGTGAAGCATTGAGCGACAAACCAGAAAACGTGCAGGAAGTCACCAACAT
CGTGAGAGGATGCTTTGAAGCTGAACAAGCCAAAGAGCATGGAAAATGTGAAAGATTTT
CCGCTTTGAGTCAATGCTACATTGAAAAGAATTTATGTCAATTCTTCTAAAATATTTTGA
AGAAAAGTTATGAATGAAAATTTTCTGAAATTTTGTTGCAAAAATATATAAATTGCCCA
ATTAAAAAAAAAAAAAAAAAAAAAAAAAAA

LJM19 (SEQ ID NO: 56)

AGTTTAATTTTCATCATGAAGTTCTTCTACTTGATTTTCTCTGCAATTTTCTTTCTGGCTGA
TCCTGCTTTGGTCAAGTGTTCAGAGGATTGTGAGAATATTTTTCATGACAATGCGTACCT
CCTTAAATTGGATTGTGAAGCAGGAAGGGTTGATCCTGTTGAATACGACGATATTTCGG
ATGAAGAAATATATGAAATAACGGTCGATGTTGGAGTTTCATCTGAGGACCAGGAGAAA
GTTGCGAAAATAATAAGGGAGTGCATTGCACAAGTTTCAACGCAAGATTGCACGAAATT
TTCAGAAATTTATGATTGTTACATGAAGAAGAAAATCTGTAATTATTATCCTGAAAATAT
GTAAAAAAAAATTATTTATTTATATAAAAAAATATAAGGATTAAAATCTCTTATTGATTG
TAAAAATGGCCTAATATTGAAGCAAAAATTAAAGCATGAAACAAGACCAAAAAAAAAA
AAAAAAAAAAAAAAAAAA

LJL138 (SEQ ID NO: 58)

TCAATCTAACAATGCACCTGCAATTGAATTTGTGCGCTATTCTCCTTTCGGTACTAAATG
GAATTCAGGGCGCTCCCAAAAGTATTAATTCAAAATCCTGCGCAATCTCCTTTCCGGAGA

ATGTAACGGCTAAGAAGGAGCCAGTGTACTTGAAACCATCAAATGATGGCTCATTGAGT
ACCCCCCTACAGCCAAGTGGGCCATTTGTAAGTCTCAAAATTGGAGAATCTCTTGCAATC
TTCTGTCCAGGTGATGGAAAGGACGTAGAGACAATTACGTGCAATACAAATTTCGATTT
AGCTTCATATTCGTGCAACAAGAGCACATCAACGGATACCATTGAAACGGAAGAAGTTT
GCGGAGGAAGTGGAAAAGTGTACAAAGTTGGTTTTCCGCTGCCCTCTGGGAATTTCCAT
TCAATCTACCAAACGTGTTTTGATAAGAAAAATCTCACACCTCTCTACTCAATTCACATT
CTCAATGGTCAAGCTGTTGGATATCACCTTAAGCACACAAGAGGAAGCTTTCGTACCAA
TGGTATCTACGGGAAAGTCAACATTGATAAACTCTACAAGACGCAAATTGAGAAATTCA
ACAAACTTTTCGGCCCTAAACAAACATTTTTCCGTAGACCCCTCAATTTTCTATCACGTG
GACACTTAAGCCCCGAAGTGGACTTTACATTCCGTAGGGAACAACATGCAACGGAAATG
TACATTAACACAGCACCACAGTACCAATCAATTAATCAAGGAAATTGGCTACGTGTTGA
AAATCACGTGAGGGATCTCGCAAAAGTTCTGCAGAAGGACATAACAGTCGTTACGGGAA
TTTTGGGGATACTTCGGTTGAAGAGTAAGAAAATAGAGAAAGAAATCTATTTAGGAGAT
GACGTAATTGCCGTACCAGCAATGTTCTGGAAGGCTGTTTTTGACCCTCAAAAACAAGA
AGCAATTGTCTTTGTTTCCTCAAATAATCCCCACGTGAAGACCTTTAATCCCAACTGCAA
GGATGTATGCGCTCAAGCTGGATTTGGGAATGATAATCTTGAATATTTCTCCAATTATTC
TATTGGTCTGACTATTTGTTGCAAACTTGAGGAATTTGTTAAAAGAAATAAAATAATTCT
ACCCAAAGAAGTAAATAACAAAAACTACACCAAAAAACTCCTTAAGTTTCCTAAAACAA
GAAACAAGGAGGGAGATAAGAAGGTGGTACGTAAGCGCGCCAAAGGAGCATAAATATT
AAACGAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

LJL15 (SEQ ID NO: 60)
GTTCTACGATAAAATTTTCTTTTCAAACTTTTCTTTTAAAGAAAAATCTTCAAAAAGTTA
AAATGAATTTGCACCTTGCGATTATCCTCTTTGTGAGTTACTTCACACTGATCACTGCTAC
GGATCTAATTGAAAAGGAACTTTCTGATTGCAAAAAGATCTTCATCTCCAAGGCTGAGC
TAACTTGGTTCCAAGCTCTCGATTTCTGTACCGAACAAAACCTAACTTTGCTCTCAATTA
AATCCGCCCGGGAAAATGATGAGGTGACTAAAGCAGTTCGAGCTGAGGTTCATCTTCCA
GACACAAAGAAGTCTCACATTTGGCTCGGAGGTATTCGTTATGATCAAGACAAGGATTT
CCGTTGGATAAGCGATGGAACAACTGTTACGAAGACAGTCTACATCAATTGGTACCAAG
GAGAACCAAATGGTGGGAGGTACCAAAAGGAATTTTGTATGGAATTGTACTTTAAAACT
CCAGCTGGTCAATGGAATGATGATATTTGTACAGCAAAGCATCATTTTATATGTCAGGA
GAAAAAATAAATTGAATTGTTCATGTGTCTTTGGCGGTGCGAAGGTATAATTCAGGTTG
ACGACATAAATTGATTTTTCTTTCATTAAGAAAATAAAGGCTTGAATTTATAAAAAAAA
AAAAAAAAAAAAAAAAAA

LJL91 (SEQ ID NO: 62)
GTTCTACGATAAAATTTTCTTTTCAAACTTTTCTTTTAAAGAAAAATCTTCAAAAAGTTA
AAATGAATTTGCCCCTTGCGATTATCCTCTTTGTGAGTTACTTCACACTGATCACTGCTGC
GGATCTAACTGAAAAGGAACTTTCTGATGGCAAAAAGATCTTCATCTCCAAGGCTGAGC

TAAGTTGGTTCGATGCTCTCGATGCCTGTACCGAAAAAGACCTAACTTTGCTCACAATTA
AATCCGCCCGGGAAAATGAGGAAGTGACTAAAGCAGTTCGAGCTGAGGTTCATCTTCCA
GACACAAAGAAGTCTCACATTTGGCTCGGAGGTATTCGTTATGATCAAGACAAGGATTT
CCGTTGGATAAGCGATGGAACAACTGTTACGAAGACAGTCTACATCAATTGGTACCAAG
GAGAACCAAATGGTGGGAGGTACCAAAAGGAATTTTGTATGGAATTGTACTTTAAAACT
CCAGCTGGTCAATGGAATGATGATATTTGTACAGCAAAGCATCATTTTATATGTCAGGA
GAAAAAATAAATTGAATTGTTCATGTGTCTTTGGCGGTGCGAAGGTATAATTCAGGTTG
ACGACATAAATTGATTTTTCTTTCATTAAGAAAATAAAGGCTTGAATTTAGCAAAAAAA
AAAAAAAAAAAAAAAAAAA

LJM11 (SEQ ID NO: 64)

TTGAATTGAAGCAGCAGCAATGAAAGTGTTTTTCTCAATTTTTACGCTCGTCCTCTTCCA
AGGGACCCTTGGAGCGGATACTCAAGGATATAAATGGAAGCAATTGCTCTACAATAATG
TTACACCAGGATCCTACAATCCGGATAATATGATCAGTACGGCTTTTGCCTACGATGCTG
AGGGTGAAAAACTCTTCCTAGCTGTCCCAAGGAAGTTACCCAGAGTTCCGTATACATTG
GCGGAAGTGGATACAAAGAATAGTCTTGGTGTTAAGGGAAAACATTCACCGTTACTTAA
CAAATTCAGTGGGCACAAAACTGGGAAGGAACTAACATCAATCTATCAGCCAGTTATTG
ATGATTGTCGTCGCCTTTGGGTGGTTGATATTGGTTCCGTGGAATATCGCTCAAGAGGTG
CCAAAGACTACCCGAGTCATCGTCCTGCAATTGTTGCGTACGACCTAAAGCAACCAAAC
TACCCCGAAGTTGTTCGATACTATTTCCCCACAAGATTAGTGGAGAAGCCAACATATTTC
GGTGGATTTGCCGTTGATGTTGCAAACCCAAAGGGGGATTGTAGTGAAACTTTTGTCTAC
ATTACAAACTTCCTCAGGGGAGCTCTCTTTATATACGATCATAAGAAGCAGGATTCGTGG
AATGTAACTCATCCCACCTTCAAAGCAGAACGACCCACTAAATTTGATTACGGCGGAAA
GGAATATGAATTCAAAGCCGGAATTTTCGGAATTACTCTCGGAGATCGAGACAGTGAAG
GCAATCGTCCAGCTTACTACTTAGCCGGAAGTGCCATCAAAGTCTACAGCGTCAACACG
AAAGAACTTAAGCAGAAGGGTGGAAAGCTGAATCCGGAGCTTCTTGGAAACCGCGGGA
AGTACAACGATGCCATTGCCCTAGCTTACGATCCCAAAACTAAAGTTATCTTCTTTGCTG
AGGCCAACACAAAGCAAGTATCCTGCTGGAACACACAGAAAATGCCACTGAGGATGAA
GAATACCGACGTAGTCTACACTAGTTCTCGCTTTGTCTTTGGAACGGACATTTCGGTTGA
TAGCAAGGGCGGCCTCTGGTTCATGTCTAACGGCTTTCCGCCTATAAGGAAATCAGAAA
AATTCAAATATGACTTCCCACGCTACCGTCTAATGAGGATCATGGACACACAGGAAGCA
ATTGCCGGAACTGCTTGCGATATGAATGCATAAAAGTTAATTTTCAACCCAAGAAGAAG
ACCTAAAGAGGCTTTTCCAGGCTTTGATGCAGGAGAGGTGGTTATCAACGCAAAATCAG
CTATTGTTGTATGAGGAGGAGAAATTATTGATTCTGAATTCTATAAAAAAAATTTAATTT
GTGAAATATTTGGCAATAATAAATTAATTGAATTACAAAAAAAAAAAAAAAAAAAAAA
AAAAAAA

LJS138 (SEQ ID NO:66)

TCTCTTTGGTTAACATTGTGAAGTTATCGGACGTGGCCGGTTTCTATTTCTTTTGCAAAAA
TGCAGTCAAAAATTCTTTCTTTCGTCCTTTTCACCTTATCCTTGGGCTATGTTTTGGGTGA
AACATGCTCAAATGCTAAGGTTAAGGGAGCTACCTCTTATTCCACAACGGATGCCACAA
TTGTAAGCCAAATTGCCTTTGTGACTGAATTCTCCTTGGAATGCTCAAATCCTGGATCCG
AGAAAATCTCCCTATTTGCTGAAGTCGATGGCAAAATTACTCCTGTTGCCATGATCGGGG
ATACCACCTACCAGGTGAGCTGGAATGAAGAGGTTAATAAGGCTAGAAGTGGTGACTAC
AGTGTGAAGCTGTACGATGAAGAAGGATACGGAGCAGTACGCAAAGCTCAGAGATCAG
GTGAAGAGAACAAGGTCAAACCACTAGCAACCGTTGTTGTTCGACATCCAGGAACATAC
ACTGGACCATGGTTCAATTCCGAAATCCTCGCAGCTGGTCTCATTGCTGTTGTTGCCTAC
TTTGCTTTCTCAACGCGAAGCAAAATTCTTTCCTAAAGAGACGCAGCATGAAATTTCACA
AAAAAATAAAAACAAATTCAAGTCATCAACCATGTCTCTTTGGCACTCAGACTGTTTCTG
TGAAATACAAACTATTATTTAACAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

LJL124 (SEQ ID NO: 68)

ATTCCCACAAGAAGCTGCTAAAATGGTGTCAATTCTGTTAATCTCCTTGATTCTTAATTT
GTTGGTTTTCTATGCTAAAGCTAGACCACTAGAAGACATCTCGTCAGATCTTTCCCCTGA
TTATTACATCACTGAAGGCTATGACGGTGTGAAGGAGAAGAGAGAGATCGAACTTGTAC
CTGTGACATTTGGAATATTTAATATACATACAACACCTGCTCCCAGAATTACCTTTGAAT
GGTAAAAAATCCAAGAAGAATTTATGATTTTATTCTTCCTTCCATTGGGATGGATTGTAA
GTCAGCATAAAACGCCGTTAAAAATGAATTTTTAATAAAAAAAAATTATTCCAAAAAAA
AAAAAAAAAAAAAAAAAAAAA

LJL35 (SEQ ID NO: 70)

CACTATTCATTGGAAGATTTATTAACTTCAAGATGAAATTATTTTGTTTAATTTTTGTTGT
GTTTGTTGCTTTAGAAGTCTGTATAGAGACCGTGAAAGCTATGGAAGCAACGGAGGAGA
TATCTGTAAAATTGCAAGATGATGCGAATGAACCTGATGACTCTCTGGATTTAGACGAA
GGTCTTCCTGATGCATTCGATGAGGACTATAATAATCAGGCTGAGTACAAGCCGAATCC
TAGAGGGGACTACAGAAGACGATAATTAATATAAATTCAGGAAAACACTCTAAAAATTT
CCAATTGACTCTACTTTAAACGATTTAATACCTACCTACACTAAATACCATATGCAATAA
TTATGTTTTAATTATTTAGTGCAAGATCTACTAGTTTCAGTTCATATTTTGGGACTTTCCC
GCCTTTCTCTCGATGGAAAAATGATTTTACGGATTCTTAATTTTCATTGTACAGAGTTAAT
AAAACAATTGAAAGCAATTAAAAAAAAAAAAAAAAAAAAAAAAAAAA

Also included are fragments of the above-described nucleic acid sequences that are at least 33 bases, at least 36 bases, at least 42 bases or at least 48 bases in length, which is sufficient to permit the fragment to selectively hybridize to a polynucleotide that encodes a disclosed *Lu. longipalpis* under specified conditions. The term "selectively hybridize" refers to hybridization under moderately or highly stringent conditions, which excludes non-related nucleotide sequences.

Also disclosed herein are open reading frames (ORFs) encoding a *Lu. longipalpis* polypeptide. These ORFs are delimited by a start codon and by a stop codon. This also includes the degenerate variants and nucleotide sequences encoding conservative variants and homologs.

Specific, non-limiting examples of open reading frames are as follows:

The LJL34 unprocessed protein is encoded by nucleic acids 30-842 of SEQ ID NO:1, and the mature protein is encoded by the nucleic acid sequence 87-842 of SEQ ID NO:1.

The LJL18 unprocessed protein is encoded by nucleic acids 56-532 of SEQ ID NO:3, and the mature protein is encoded by the nucleic acid sequence 113-532 of SEQ ID NO:3.

The LJS193 unprocessed protein is encoded by nucleic acids 216-502 of SEQ ID NO:5, and the mature protein is encoded by the nucleic acid sequence 276-502 of SEQ ID NO:5.

The LJS201 unprocessed protein is encoded by nucleic acids 48-353 of SEQ ID NO:7, and the mature protein is encoded by the nucleic acid sequence 117-352 of SEQ ID NO:7.

The LJL13 unprocessed protein is encoded by nucleic acids 26-766 of SEQ ID NO:9, and the mature protein is encoded by the nucleic acid sequence 83-766 of SEQ ID NO:9.

The LJL23 unprocessed protein is encoded by nucleic acids 18-992 of SEQ ID NO:11, and the mature protein is encoded by the nucleic acid sequence 81-992 of SEQ ID NO:11.

The LJM10 unprocessed protein is encoded by nucleic acids 92-571 of SEQ ID NO:13, and the mature protein is encoded by the nucleic acid sequence 149-571 of SEQ ID NO:13.

The LJL143 unprocessed protein is encoded by nucleic acids 46-948 of SEQ ID NO:15, and the mature protein is encoded by the nucleic acid sequence 115-948 of SEQ ID NO:15.

The LJS142 unprocessed protein is encoded by nucleic acids 25-507 of SEQ ID NO:17, and the mature protein is encoded by the nucleic acid sequence 85-507 of SEQ ID NO: 17.

The LJL17 unprocessed protein is encoded by nucleic acids 28-342 of SEQ ID NO:19, and the mature protein is encoded by the nucleic acid sequence 88-342 of SEQ ID NO:19.

The LJM06 unprocessed protein is encoded by nucleic acids 50-523 of SEQ ID NO:21, and the mature protein is encoded by the nucleic acid sequence 107-523 of SEQ ID NO:21.

The LJM17 unprocessed protein is encoded by nucleic acids 24-1264 of SEQ ID NO:23, and the mature protein is encoded by the nucleic acid sequence 83-1264 of SEQ ID NO:23.

The LJL04 unprocessed protein is encoded by nucleic acids 30-914 of SEQ ID NO:25, and the mature protein is encoded by the nucleic acid sequence 81-914 of SEQ ID NO:25.

The LJM114 unprocessed protein is encoded by nucleic acids 29-475 of SEQ ID NO:27, and the mature protein is encoded by the nucleic acid sequence 101-475 of NO:27.

The LJM111 unprocessed protein is encoded by nucleic acids 24-1214 of SEQ ID NO:29, and the mature protein is encoded by the nucleic acid sequence 78-1214 of SEQ ID NO:29.

The LJM78mature unprocessed protein is encoded by nucleic acids 42-1091 of SEQ ID NO:31, and the mature protein is encoded by the nucleic acid sequence 102-11091 of SEQ ID NO:31.

The LJS238 unprocessed protein is encoded by nucleic acids 27-206 of SEQ ID NO:33, and the mature protein is encoded by the nucleic acid sequence 87-206 of SEQ ID NO:33.

The LJS169 unprocessed protein is encoded by nucleic acids 11-370 of SEQ ID NO:35, and the mature protein is encoded by the nucleic acid sequence 77-370 of SEQ ID NO:35.

The LJL11 unprocessed protein is encoded by nucleic acids 30-1745 of SEQ ID NO:37, and the mature protein is encoded by the nucleic acid sequence 105-1745 of SEQ ID NO:37.

The LJL08 unprocessed protein is encoded by nucleic acids 26-238 of SEQ ID NO:39, and the mature protein is encoded by the nucleic acid sequence 95-238 of SEQ ID NO:39.

The LJS105 unprocessed protein is encoded by nucleic acids 24-275 of SEQ ID NO:41, and the mature protein is encoded by the nucleic acid sequence 81-275 of SEQ ID NO:41.

The LJL09 unprocessed protein is encoded by nucleic acids 74-1954 of SEQ ID NO:43, and the mature protein is encoded by the nucleic acid sequence 128-1954 of SEQ ID NO:43.

The LJL38 unprocessed protein is encoded by nucleic acids 40-165 of SEQ ID NO:45, and the mature protein is encoded by the nucleic acid sequence 100-165 of SEQ ID NO:45.

The LJM04 unprocessed protein is encoded by nucleic acids 40-456 of SEQ ID NO:47, and the mature protein is encoded by the nucleic acid sequence 100-456 of SEQ ID NO:47.

The LJM26 unprocessed protein is encoded by nucleic acids 96-1616 of SEQ ID NO:49, and the mature protein is encoded by the nucleic acid sequence 147-1616 of SEQ ID NO:49.

The LJS03 unprocessed protein is encoded by nucleic acids 41-553 of SEQ ID NO:51, and the mature protein is encoded by the nucleic acid sequence 98-553 of SEQ ID NO:51.

The LJS192 unprocessed protein is encoded by nucleic acids 18-344 of SEQ ID NO:53, and the mature protein is encoded by the nucleic acid sequence 87-344 of SEQ ID NO:53.

The LJM19 unprocessed protein is encoded by nucleic acids 16-360 of SEQ ID NO:55, and the mature protein is encoded by the nucleic acid sequence 82-360 of SEQ ID NO:55.

The LJL138 unprocessed protein is encoded by nucleic acids 12-1238 of SEQ ID NO:57 and the mature protein is encoded by the nucleic acid sequence 72-1238 of SEQ ID NO:57.

The LJL15 unprocessed protein is encoded by nucleic acids 63-542 of SEQ ID NO:59, and the mature protein is encoded by the nucleic acid sequence 120-542 of SEQ ID NO:59.

The LJL91 unprocessed protein is encoded by nucleic acids 63-542 of SEQ ID NO:61, and the mature protein is encoded by the nucleic acid sequence 120-542 of SEQ ID NO:61.

The LJM11unprocessed protein is encoded by nucleic acids 20-1216 of SEQ ID NO:63, and the mature protein is encoded by the nucleic acid sequence 74-1216 of SEQ ID NO:63.

The LJS138 unprocessed protein is encoded by nucleic acids 12-1238 of SEQ ID NO:65, and the mature protein is encoded by the nucleic acid sequence 72-138 of SEQ ID NO:65.

The LJL124 unprocessed protein is encoded by nucleic acids 23-241 of SEQ ID NO:67, and the mature protein is encoded by the nucleic acid sequence 83-241 of SEQ ID NO:67.

The LJL35 unprocessed protein is encoded by nucleic acids 12-1238 of SEQ ID NO:69, and the mature protein is encoded by the nucleic acid sequence 72-1238 of SEQ ID NO:69.

Another specific non-limiting example of a polynucleotide encoding a *Lu. longipalpis* polypeptide is a polynucleotide having at least 75%, 85%, 90%, 95%, or 99% homology to one of the

sequences set forth above that encodes a polypeptide having an antigenic epitope or function of a *Lu. longipalpis* polypeptide. Yet another specific non-limiting example of a polynucleotide encoding a *Lu. longipalpis* polypeptide is a polynucleotide that encodes a polypeptide that is specifically bound by an antibody that specifically binds the *Lu. longipalpis* polypeptide.

The *Lu. longipalpis* polynucleotides include a recombinant DNA which is incorporated into a vector, into an autonomously replicating plasmid or virus, or into the genomic DNA of a prokaryote or eukaryote, or which exists as a separate molecule (for example, a cDNA) independent of other sequences. The nucleotides can be ribonucleotides, deoxyribonucleotides, or modified forms of either nucleotide. The term includes single and double forms of either nucleotide. The term includes single and double forms of DNA.

Recombinant vectors are also disclosed herein that include a polynucleotide encoding a polypeptide or a fragment thereof according to the disclosure. Recombinant vectors include plasmids and viral vectors and may be used for *in vitro* or *in vivo* expression.

A plasmid may include a DNA transcription unit, for instance a nucleic acid sequence that permit it to replicate in a host cell, such as an origin of replication (prokaryotic or eukaryotic). A plasmid may also include one or more selectable marker genes and other genetic elements known in the art. Circular and linear forms of plasmids are encompassed in the present disclosure.

For *in vivo* expression, the promoter is generally of viral or cellular origin. In one embodiment, the cytomegalovirus (CMV) early promoter (CMV-IE promoter), including the promoter and enhancer, is of use. The CMV-IE promoter can be of human or murine origin, or of other origin such as rat or guinea pig (see EP 0260148; EP 0323597; WO 89/01036; Pasleau *et al.*, *Gene* 38:227-232, 1985; Boshart M. *et al.*, *Cell* 41:521-530, 1985). Functional fragments of the CMV-IE promoter may also be used (WO 98/00166). The SV40 virus early or late promoter and the Rous Sarcoma virus LTR promoter are also of use. Other promoters include but are not limited to, a promoter of a cytoskeleton gene, such as (but not limited to) the desmin promoter (Kwissa M. *et al.*, *Vaccine* 18(22):2337-2344, 2000), or the actin promoter (Miyazaki J. *et al.*, *Gene* 79(2):269-277, 1989). When several genes are present in the same plasmid, they may be provided in the same transcription unit or in different units.

The plasmids may also comprise other transcription regulating elements such as, for example, stabilizing sequences of the intron type. In several embodiments the plasmids include the first intron of CMV-IE (Published PCT Application No. WO 89/01036), the intron II of the rabbit β-globin gene (van Ooyen *et al.*, *Science* 206:337-344, 1979), the signal sequence of the protein encoded by the tissue plasminogen activator (tPA; Montgomery *et al.*, *Cell. Mol. Biol.* 43:285-292, 1997), and/or a polyadenylation signal (polyA), in particular the polyA of the bovine growth hormone (bGH) gene (U.S. Patent No. 5,122,458) or the polyA of the rabbit β-globin gene or of SV40 virus.

In a specific, non-limiting example, the pVR1020 plasmid (VICAL Inc.; Luke C. *et al.*, *Journal of Infectious Diseases* 175:91-97, 1997; Hartikka J. *et al.*, *Human Gene Therapy* 7:1205-

1217, 1996)) can be utilized as a vector for the insertion of such a polynucleotide sequence, generating recombinant plasmids.

The plasmids are evaluated in dogs in order to determine their efficacy against a Leishmania infection (Vidor E. *et al.*, P3.14, XXIV World Veterinary Congress, Rio de Janeiro, Brazil, 18-23 August 1991).

Various viral vectors are also of use with a polynucleotide encoding a *Lu. longipalpis* polypeptide. A specific, non-limiting example includes recombinant poxvirus, including avipox viruses, such as the canarypox virus. Another specific, non-limiting example includes recombinant poxvirus, including vaccinia viruses (U.S. Patent No. 4,603,112), such as attenuated vaccinia virus such as NYVAC (see U.S. Patent No. 5,494,807) or Modified Vaccinia virus Ankara (MVA, Stickl H. and Hochstein-Mintzel V., *Munch. Med. Wschr.* 113:1149-1153, 1971; Sutter G. *et al.*, *Proc. Natl. Acad. Sci. USA* 89:10847-10851, 1992; Carroll M. W. *et al.*, *Vaccine* 15(4):387-394, 1997; Stittelaar K. J. *et al.*, *J. Virol.* 74(9):4236-4243, 2000; Sutter G. *et al.*, *Vaccine* 12(11):1032-1040, 1994). When avipox viruses are used, canarypox viruses (U.S. Patent No. 5,756,103) and fowlpox viruses (U.S. Patent No. 5,766,599) are of use, such as attenuated viruses. For recombinant canarypox virus vectors, the insertion sites may be in particular in the ORFs C3, C5 or C6. When the expression vector is a poxvirus, the heterologous polynucleotide can be inserted under the control of a poxvirus specific promoter, such as the vaccinia virus 7.5kDa promoter (Cochran *et al.*, *J. Virology* 54:30-35, 1985), the vaccinia virus I3L promoter (Riviere *et al.*, *J. Virology* 66:3424-3434, 1992), the vaccinia virus HA promoter (Shida, *Virology* 150:451-457, 1986), the cowpox virus ATI promoter (Funahashi *et al.*, *J. Gen. Virol.* 69:35-47, 1988), other vaccinia virus H6 promoter (Taylor *et al.*, *Vaccine* 6:504-508, 1988; Guo *et al.*, *J. Virol.* 63:4189-4198, 1989; Perkus *et al.*, *J. Virol.* 63:3829-3836, 1989).

Other viral vectors of use are herpes virus or adenovirus vectors. Specific, non-limiting examples include a canine herpes virus (CHV) or canine adenovirus (CAV) vector (for example, see U.S. Patent No. 5,529,780; U.S. Patent No. 5,688,920; Published PCT Application No. WO 95/14102). For CHV, the insertion sites may be in particular in the thymidine kinase gene, in the ORF3, or in the UL43 ORF (see U.S. Patent No. 6,159,477). For CAV, the insertion sites may be in particular in the E3 region or in the region located between the E4 region and the right ITR region (see U.S. Patent No. 6,090,393; U.S. Patent No. 6,156,567). In one embodiment in CHV or CAV vectors the insert is in general under the control of a promoter (as described above for the plasmids), such as CMV-IE promoter.

Multiple insertions can be done in the same vector using different insertion sites or using the same insertion site. When the same insertion site is used, each polynucleotide insert is inserted under the control of different promoters. The insertion can be done tail-to-tail, head-to-head, tail-to-head, or head-to-tail. IRES elements (Internal Ribosome Entry Site, see European Patent EP 0803573) can also be used to separate and to express multiple inserts operably linked to the same promoter. Bacterial vectors can also be used for *in vivo* expression.

Any polynucleotide according to the disclosure can be expressed *in vitro* by DNA transfer or expression vectors into a suitable host cell. The host cell may be prokaryotic or eukaryotic. The term "host cell" also includes any progeny of the subject host cell. Methods of stable transfer, meaning that the foreign polynucleotide is continuously maintained in the host cell, are known in the art. Host cells can include bacteria (for example, *Escherichia coli*), yeast, insect cells, and vertebrate cells. Methods of expressing DNA sequences in eukaryotic cells are well known in the art.

As a method for *in vitro* expression, recombinant Baculovirus vectors (for example, Autographa California Nuclear Polyhedrosis Virus (AcNPV)) can be used with the nucleic acids disclosed herein. For example, polyhedrin promoters can be utilized with insect cells (for example, *Spodoptera frugiperda* cells, like Sf9 cells available at the ATCC under the Accession number CRL-1711, or Sf21 cells) (see for example, Smith *et al.*, *Mol. Cell Biol.* 3:2156-2165, 1983; Pennock *et al.*, *Mol. Cell Biol.* 4: 399-406, 1994; Vialard *et al.*, *J. Virol.* 64:37-50, 1990; Verne A., *Virology* 167:56-71, 1988; O'Reilly *et al.*, "Baculovirus expression vectors, A laboratory manual," New York Oxford, Oxford University Press, 1994; Kidd I. M. & Emery V.C., "The use of baculoviruses as expression vectors," *Applied Biochemistry and Biotechnology* 42:37-159, 1993; European Patent No. EP 0370573; European Patent No. EP 0265785; U.S. Patent No. 4,745,051). For expression the BaculoGold ™ Starter Package (Cat # 21001K) from Pharmingen (Becton Dickinson) can be used.

As a method for *in vitro* expression, recombinant *E. coli* can be used with a vector. For example, when cloning in bacterial systems, inducible promoters such as arabinose promoter, pL of bacteriophage lambda, plac, ptrp, ptac (ptrp-lac hybrid promoter), and the like may be used.

Transformation of a host cell with recombinant DNA may be carried out by conventional techniques as are well known to those skilled in the art. Where the host is prokaryotic, such as *E. coli*, competent cells which are capable of DNA uptake can be prepared from cells harvested after exponential growth phase and subsequently treated by the $CaCl_2$ method using procedures well known in the art. Alternatively, $MgCl_2$ or RbCl can be used. Transformation can also be performed after forming a protoplast of the host cell if desired, or by electroporation.

When the host is a eukaryote, such methods of transduction of DNA as calcium phosphate coprecipitates, conventional mechanical procedures such as microinjection, electroporation, insertion of a plasmid encased in liposomes, or virus vectors may be used. Eukaryotic cells can also be cotransformed with *Lu. longipalpis* polynucleotide sequences, and a second foreign DNA molecule encoding a selectable phenotype, such as the herpes simplex thymidine kinase gene. Another method is to use a eukaryotic viral vector (see above), such as a herpes virus or adenovirus (for example, canine adenovirus 2), to transiently transduce eukaryotic cells and express the protein (see for example, *Eukaryotic Viral Vectors*, Cold Spring Harbor Laboratory, Gluzman ed., 1982). In addition, a transfection agent can be utilized, such as dioleoyl-phosphatidyl-ethanolamine (DOPE).

Isolation and purification of recombinantly expressed polypeptide may be carried out by conventional means including preparative chromatography (for example, size exclusion, ion exchange, affinity), selective precipitation and ultra-filtration. Such a recombinantly expressed polypeptide is part of the present disclosure. The methods for production of such a polypeptide are

also encompassed, in particular the use of a recombinant expression vector comprising a polynucleotide according to the disclosure and of a host cell.

Antibodies

A *Lu. longipalpis* polypeptide of the disclosure or a fragment thereof according to the disclosure can be used to produce antibodies. Polyclonal antibodies, antibodies which consist essentially of pooled monoclonal antibodies with different epitopic specificities, as well as distinct monoclonal antibodies are included. Such antibodies are of use as markers for exposure, and as immunodiagnostic tools to follow the development of the immune response to *Lu. longipalpis* salivary proteins.

The preparation of polyclonal antibodies is well-known to those skilled in the art. See, for example, Green et al., "Production of Polyclonal Antisera," *Immunochemical Protocols*, pp. 1-5, Manson, ed., *Humana Press*, 1992; Coligan *et al.*, "Production of Polyclonal Antisera in Rabbits, Rats, Mice and Hamsters," *Current Protocols in Immunology*, section 2.4.1, 1992.

The preparation of monoclonal antibodies likewise is conventional. See, for example, Kohler & Milstein, *Nature* 256:495, 1975; Coligan *et al.*, sections 2.5.1-2.6.7; and Harlow *et al.*, *Antibodies: A Laboratory Manual*, p. 726, Cold Spring Harbor Pub., 1988. Briefly, monoclonal antibodies can be obtained by injecting mice with a composition comprising an antigen, verifying the presence of antibody production by removing a serum sample, removing the spleen to obtain B lymphocytes, fusing the B lymphocytes with myeloma cells to produce hybridomas, cloning the hybridomas, selecting positive clones that produce antibodies to the antigen, and isolating the antibodies from the hybridoma cultures. Monoclonal antibodies can be isolated and purified from hybridoma cultures by a variety of well-established techniques. Such isolation techniques include affinity chromatography with Protein-A Sepharose, size-exclusion chromatography, and ion-exchange chromatography. See, for example, Coligan *et al.*, sections 2.7.1-2.7.12 and sections 2.9.1-2.9.3; Barnes *et al.*, "Purification of Immunoglobulin G (IgG)," *Methods in Molecular Biology*, Vol. 10, pp. 79-104, Humana Press, 1992.

Methods of *in vitro* and *in vivo* multiplication of monoclonal antibodies are well known to those skilled in the art. Multiplication *in vitro* may be carried out in suitable culture media such as Dulbecco's Modified Eagle Medium or RPMI 1640 medium, optionally supplemented by a mammalian serum such as fetal calf serum or trace elements and growth-sustaining supplements such as normal mouse peritoneal exudate cells, spleen cells, thymocytes, or bone marrow macrophages. Production *in vitro* provides relatively pure antibody preparations and allows scale-up to yield large amounts of the desired antibodies. Large-scale hybridoma cultivation can be carried out by homogenous suspension culture in an airlift reactor, in a continuous stirrer reactor, or in immobilized or entrapped cell culture. Multiplication *in vivo* may be carried out by injecting cell clones into mammals histocompatible with the parent cells, for example, syngeneic mice, to cause growth of antibody-producing tumors. Optionally, the animals are primed with a hydrocarbon, especially oils

such as pristane (tetramethylpentadecane) prior to injection. After one to three weeks, the desired monoclonal antibody is recovered from the body fluid of the animal.

Antibodies can also be derived from subhuman primate antibody. General techniques for raising therapeutically useful antibodies in baboons can be found, for example, in WO 91/11465, 1991, and Losman *et al.*, *Int. J. Cancer* 46:310, 1990.

Alternatively, an antibody that specifically binds a polypeptide can be derived from a humanized monoclonal antibody. Humanized monoclonal antibodies are produced by transferring mouse complementarity determining regions from heavy and light variable chains of the mouse immunoglobulin into a human variable domain, and then substituting human residues in the framework regions of the murine counterparts. The use of antibody components derived from humanized monoclonal antibodies obviates potential problems associated with the immunogenicity of murine constant regions. General techniques for cloning murine immunoglobulin variable domains are described, for example, by Orlandi *et al.*, *Proc. Nat'l Acad. Sci. USA* 86:3833, 1989. Techniques for producing humanized monoclonal antibodies are described, for example, by Jones *et al.*, *Nature* 321:522, 1986; Riechmann *et al.*, *Nature* 332:323, 1988; Verhoeyen *et al.*, *Science* 239:1534, 1988; Carter *et al.*, *Proc. Nat'l Acad. Sci. USA* 89:4285, 1992; Sandhu, *Crit. Rev. Biotech.* 12:437, 1992; and Singer *et al.*, *J. Immunol.* 150:2844, 1993.

Antibodies can be derived from human antibody fragments isolated from a combinatorial immunoglobulin library. See, for example, Barbas *et al.*, *Methods: a Companion to Methods in Enzymology*, Vol. 2, p. 119, 1991; Winter *et al.*, *Ann. Rev. Immunol.* 12:433, 1994. Cloning and expression vectors that are useful for producing a human immunoglobulin phage library can be obtained, for example, from STRATAGENE Cloning Systems (La Jolla, CA).

In addition, antibodies can be derived from a human monoclonal antibody. Such antibodies are obtained from transgenic mice that have been "engineered" to produce specific human antibodies in response to antigenic challenge. In this technique, elements of the human heavy and light chain loci are introduced into strains of mice derived from embryonic stem cell lines that contain targeted disruptions of the endogenous heavy and light chain loci. The transgenic mice can synthesize human antibodies specific for human antigens, and the mice can be used to produce human antibody-secreting hybridomas. Methods for obtaining human antibodies from transgenic mice are described by Green *et al.*, *Nature Genet.* 7:13, 1994; Lonberg *et al.*, *Nature* 368:856, 1994; and Taylor *et al.*, *Int. Immunol.* 6:579, 1994.

Antibodies include intact molecules as well as fragments thereof, such as Fab, $F(ab')_2$, and Fv which are capable of binding the epitopic determinant. These antibody fragments retain some ability to selectively bind with their antigen or receptor and are defined as follows:

(1) Fab, the fragment which contains a monovalent antigen-binding fragment of an antibody molecule, can be produced by digestion of whole antibody with the enzyme papain to yield an intact light chain (L) and a portion of one heavy chain(H);

(2) Fab', the fragment of an antibody molecule that can be obtained by treating a whole antibody with pepsin, followed by reduction, to yield an intact light chain and a portion of the heavy chain; two Fab' fragments are obtained per antibody molecule;

(3) $(Fab')_2$, the fragment of the antibody that can be obtained by treating a whole antibody with the enzyme pepsin without subsequent reduction; $F(ab')_2$ is a dimer of two Fab' fragments held together by two disulfide bonds;

(4) Fv, defined as a genetically engineered fragment containing the variable region of the light chain (V_L) and the variable region of the heavy chain (V_H) expressed as two chains; and

(5) Single chain antibody (SCA), defined as a genetically engineered molecule containing the variable region of the light chain, the variable region of the heavy chain, linked by a suitable polypeptide linker as a genetically fused single chain molecule.

Methods of making these fragments are known in the art. (See for example, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, New York, 1988).

Antibody fragments can be prepared by proteolytic hydrolysis of the antibody or by expression in *E. coli* of DNA encoding the fragment. Antibody fragments can be obtained by pepsin or papain digestion of whole antibodies by conventional methods. For example, antibody fragments can be produced by enzymatic cleavage of antibodies with pepsin to provide a 5S fragment denoted $F(ab')_2$. This fragment can be further cleaved using a thiol reducing agent, and optionally a blocking group for the sulfhydryl groups resulting from cleavage of disulfide linkages, to produce 3.5S Fab' monovalent fragments. Alternatively, an enzymatic cleavage using pepsin produces two monovalent Fab' fragments and an Fc fragment directly (see U.S. Patent No. 4,036,945 and U.S. Patent No. 4,331,647, and references contained therein; Nisonhoff *et al.*, *Arch. Biochem. Biophys.* 89:230, 1960; Porter, *Biochem. J.* 73:119, 1959; Edelman *et al.*, *Methods in Enzymology*, Vol. 1, page 422, Academic Press, 1967; and Coligan *et al.* at sections 2.8.1-2.8.10 and 2.10.1-2.10.4).

Other methods of cleaving antibodies, such as separation of heavy chains to form monovalent light-heavy chain fragments, further cleavage of fragments, or other enzymatic, chemical, or genetic techniques may also be used, so long as the fragments bind to the antigen that is recognized by the intact antibody.

For example, Fv fragments comprise an association of V_H and V_L chains. This association may be noncovalent (Inbar *et al.*, *Proc. Nat'l Acad. Sci. USA* 69:2659, 1972). Alternatively, the variable chains can be linked by an intermolecular disulfide bond or cross-linked by chemicals such as glutaraldehyde. See, for example, Sandhu, *supra*. In one embodiment, the Fv fragments comprise V_H and V_L chains connected by a peptide linker. These single-chain antigen binding proteins (sFv) are prepared by constructing a structural gene comprising DNA sequences encoding the V_H and V_L domains connected by an oligonucleotide. The structural gene is inserted into an expression vector, which is subsequently introduced into a host cell such as *E. coli*. The recombinant host cells synthesize a single polypeptide chain with a linker peptide bridging the two V domains. Methods for producing sFvs are known in the art (see Whitlow *et al.*, *Methods: a Companion to Methods in*

Enzymology, Vol. 2, page 97, 1991; Bird *et al.*, *Science* 242:423, 1988; U.S. Patent No. 4,946,778; Pack *et al.*, *Bio/Technology* 11:1271, 1993; and Sandhu, *supra)*.

Another form of an antibody fragment is a peptide coding for a single complementarity-determining region (CDR). CDR peptides ("minimal recognition units") can be obtained by constructing genes encoding the CDR of an antibody of interest. Such genes are prepared, for example, by using the polymerase chain reaction to synthesize the variable region from RNA of antibody-producing cells (Larrick *et al.*, *Methods: a Companion to Methods in Enzymology*, Vol. 2, page 106, 1991).

Antibodies can be prepared using an intact polypeptide or fragments containing small peptides of interest as the immunizing antigen. The polypeptide or a peptide used to immunize an animal can be derived from substantially purified polypeptide produced in host cells, *in vitro* translated cDNA, or chemical synthesis which can be conjugated to a carrier protein, if desired. Such commonly used carriers which are chemically coupled to the peptide include keyhole limpet hemocyanin (KLH), thyroglobulin, bovine serum albumin (BSA), and tetanus toxoid. The coupled peptide is then used to immunize an animal (for example, a mouse, a rat, or a rabbit).

Polyclonal or monoclonal antibodies can be further purified, for example, by binding to and elution from a matrix to which the polypeptide or a peptide to which the antibodies were raised is bound. Those of skill in the art will know of various techniques common in the immunology arts for purification and/or concentration of polyclonal antibodies, as well as monoclonal antibodies (See for example, Coligan *et al.*, Unit 9, *Current Protocols in Immunology*, Wiley Interscience, 1991).

It is also possible to use the anti-idiotype technology to produce monoclonal antibodies which mimic an epitope. For example, an anti-idiotypic monoclonal antibody made to a first monoclonal antibody will have a binding domain in the hypervariable region that is the "image" of the epitope bound by the first mono-clonal antibody.

In view of the large number of methods that have been reported for attaching a variety of radiodiagnostic compounds, radiotherapeutic compounds, label (for example, enzymes or fluorescent molecules) drugs, toxins, and other agents to antibodies one skilled in the art will be able to determine a suitable method for attaching a given agent to an antibody or other polypeptide.

In one embodiment, an antibody that binds a *Lu. Longipalpis* polypeptide can be used to assess whether a subject has been bitten by a sand fly. In one specific, non-limiting example, a sample is obtained from a subject of interest, such as a human or a dog. The sample can be a body fluid (for example, blood, serum, urine, saliva, etc.) or a tissue biopsy. The sample or a fraction thereof is contacted with the antibody, and the ability of the antibody to form an antigen-antibody complex is assessed. One of skill in the art can readily detect the formation of an antigen-antibody complex. For example, ELISA, Western blot, or radio-immune assays can be utilized.

Immunogenic Compositions, Vaccines and Methods of Use

Immunogenic compositions and vaccines are disclosed herein. In one embodiment the immunogenic compositions and vaccines include a polypeptide. In another embodiment, the

immunogenic compositions and vaccines include a recombinant vector, such as a viral vector or a plasmid. When administered to a subject such an immunogenic composition or vaccine generates an immune response to the sand fly's salivary protein(s), and surprisingly a reduction of the leishmaniasis symptoms and a decrease of the leishmania parasite load results. Thus, without being bound by theory, a cellular response, such as a Th1 response, produced against the salivary protein can indirectly kill a Leishmania parasite. For example, a Th1 type response can allow macrophages to take up Leishmania antigens and present them to T cells in a Th1 context. The induction the Th1 response can produce an anti-Leishmania immune response, or can prime the immune system of the mammalian host for anti-Leishmania immunity in response to a later infection.

In one embodiment, the immunogenic composition or the vaccine includes an effective amount of at least one *Lu. longipalpis* polypeptide disclosed herein. The immunogenic composition and the vaccine can include a pharmaceutically acceptable excipient and/or an adjuvant. In one embodiment, the immunogenic composition or vaccine includes a polypeptide having an amino acid sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, a polypeptide at least 80%, at least 90%, at least 95%, or at least 99% homologous to one of these polypeptides, a conservative variant, a homolog or an immunogenic fragment comprising at least eight or at least ten consecutive amino acids of one of these polypeptides, or a combination of these polypeptides. In one specific, non-limiting example, the immunogenic composition or vaccine includes a polypeptide having an amino acid sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67. In specific, non-limiting examples, the immunogenic composition includes a polypeptide having a sequence set forth as one of SEQ ID NO: 3, SEQ ID NO: 11, SEQ ID NO: 19, SEQ ID NO: 29, SEQ ID NO: 55, or SEQ ID NO: 59.

In one embodiment, the immunogenic composition includes more than one *Lu. longipalpis* polypeptide, such as two, three, four, five, six, ten or more of the polypeptides disclosed herein. Thus, the immunogenic composition includes at least one polypeptide having an amino acid sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, a polypeptide at least 80%, at least 90%, at least 95%, or at least 99% homologous to one of these

polypeptides, a conservative variant, a homolog or an immunogenic fragment comprising at least eight or at least ten consecutive amino acids of one of these polypeptides, and optionally another polypeptide having an amino acid sequence as set forth as SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, or SEQ ID NO: 69, a polypeptide at least 80%, at least 90%, at least 95%, or at least 99% homologous to one of these polypeptides, a conservative variant of one of these polypeptides, or a homolog or an immunogenic fragment comprising at least eight or at least ten consecutive amino acids of one of these polypeptides.

In specific non-limiting examples, the immunogenic composition includes an amino acid having a sequence as set forth as SEQ ID NO: 1, SEQ ID NO: 23, SEQ ID NO: 39, a polypeptide at least 80%, at least 90%, at least 95%, or at least 99% homologous to one of these polypeptides, a conservative variant of one of these polypeptides, or a homolog or an immunogenic fragment comprising at least eight or at least ten consecutive amino acids of one of these polypeptides, or a combination of these polypeptides. Thus, the immunogenic composition can include a polypeptide having a sequence as set forth as SEQ ID NO: 1, SEQ ID NO: 23, or SEQ ID NO: 39. These compositions include, but are not limited to, an immunogenic composition including a polypeptide having a sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 11, SEQ ID NO: 19, SEQ ID NO: 29, SEQ ID NO: 55, or SEQ ID NO: 59, and a polypeptide having a sequence as set forth as SEQ ID NO: 1, SEQ ID NO: 23, or SEQ ID NO: 39.

The immunogenic composition or the vaccine can include a pharmaceutically acceptable excipient and/or an adjuvant.

In another embodiment, the immunogenic composition or the vaccine includes an effective amount of at least one *Lu. longipalpis* polypeptide in conjunction with one or more *P. perniciosus* polypeptide(s) and/or one or more *P. ariasi* polyeptide(s). These polypeptide sequences are disclosed in U.S. Patent Application No. 60/412,327, filed September 19, 2002, U.S. Patent Application No. 60/425,852, filed November 12, 2002, and PCT Application No. PCT/US03/29833, filed September 18, 2003, which are incorporated herein by reference.

In one embodiment, the immunogenic composition or the vaccine comprises an effective amount of a recombinant vector expressing at least one *Lu. longipalpis* polypeptide disclosed herein and a pharmaceutically acceptable vehicle or excipient. In one specific, non-limiting example the recombinant vector encodes at least one polypeptide having an amino acid sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ

ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, a conservative variant, a homolog, an immunogenic fragment, or a fusion protein thereof. In specific non-limiting examples the vector encodes a polypeptide having a sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 11, SEQ ID NO: 19, SEQ ID NO: 29, SEQ ID NO: 55, or SEQ ID NO: 59, a polypeptide at least 80%, at least 90%, at least 95%, or at least 99% homologous to one of these polypeptides, a conservative variant, a homolog, an immunogenic fragment, or a fusion protein thereof. In several examples the vector encodes one or more polypeptides having a sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 11, SEQ ID NO: 19, SEQ ID NO: 29, SEQ ID NO: 55, or SEQ ID NO: 59. The vector can also optionally encode a polypeptide having a sequence as set forth as SEQ ID NO: 1, SEQ ID NO: 23, or SEQ ID NO: 39.

The immunogenic composition can include a nucleic acid sequence encoding a *P. ariasi* polypeptide(s) and/or a *P. perniciosus* polypeptide(s) (see U.S. Provisional Application No. 60/412,327, which is incorporated by reference herein in its entirety). In one embodiment, the *Lu. longipalpis* polypeptide(s) having an amino acid sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, a conservative variant, a homolog, an immunogenic fragment, or a fusion protein thereof, are encoded by the same recombinant vector as a *P. ariasi* polypeptide(s) and/or a *P. perniciosus* polypeptide(s). In another embodiment, the *Lu. longipalpis* polypeptide(s), a *P. ariasi* polypeptide(s) and/or a *P. perniciosus* polypeptide(s), are encoded by different recombinant vectors.

The *Lu. longipalpis* polypeptide can be administered by any means known to one of skill in the art (See Banga, A., "Parenteral Controlled Delivery of Therapeutic Peptides and Proteins," *Therapeutic Peptides and Proteins*, Technomic Publishing Co., Inc., Lancaster, PA, 1995) such as by intramuscular (IM), intradermal (ID), subcutaneous (SC), or intravenous injection, but even oral, nasal, or anal administration is contemplated. In one embodiment, administration is by subcutaneous, intradermal, or intramuscular injection using a needleless injector (Biojector™, Bioject, Oregon, USA).

To extend the time during which the peptide or protein is available to stimulate a response, the peptide or protein can be provided as an implant, an oily injection, or as a particulate system. The particulate system can be a microparticle, a microcapsule, a microsphere, a nanocapsule, or similar particle. (see, for example, Banja, *supra)*. A particulate carrier based on a synthetic polymer has been shown to act as an adjuvant to enhance the immune response, in addition to providing a controlled release. Aluminum salts may also be used as adjuvants to produce a humoral immune response. Thus, in one embodiment, a *Lu. longipalpis* polypeptide is administered in a manner to induce a humoral response.

In another embodiment, a *Lu. longipalpis* polypeptide is administered in a manner to direct the immune response to a cellular response (that is, a CTL response), rather than a humoral (antibody) response. A number of means for inducing cellular responses, both *in vitro* and *in vivo*, are known. Lipids have been identified as agents capable of assisting in priming CTL *in vivo* against various antigens. For example, as described in U.S. Patent No. 5,662,907, palmitic acid residues can be attached to the alpha and epsilon amino groups of a lysine residue and then linked (for example, via one or more linking residues, such as glycine, glycine-glycine, serine, serine-serine, or the like) to an immunogenic peptide. The lipidated peptide can then be injected directly in a micellar form, incorporated in a liposome, or emulsified in an adjuvant. As another example, *E. coli* lipoproteins, such as tripalmitoyl-S-glycerylcysteinylseryl-serine can be used to prime tumor specific CTL when covalently attached to an appropriate peptide (see, Deres *et al.*, *Nature* 342:561, 1989). Further, as the induction of neutralizing antibodies can also be primed with the same molecule conjugated to a peptide which displays an appropriate epitope, the two compositions can be combined to elicit both humoral and cell-mediated responses where that is deemed desirable.

In yet another embodiment, an MHC class II-restricted T-helper epitope is added to the polypeptide of the disclosure to induce T-helper cells to secrete cytokines in the microenvironment to activate CTL precursor cells. The technique further involves adding short lipid molecules to retain the construct at the site of the injection for several days to localize the antigen at the site of the injection and enhance its proximity to dendritic cells or other "professional" antigen presenting cells over a period of time (see Chesnut *et al.*, "Design and Testing of Peptide-Based Cytotoxic T-Cell-Mediated Immunotherapeutics to Treat Infectious Diseases and Cancer," Powell, *et al.*, (eds.), *Vaccine Design, the Subunit and Adjuvant Approach*, Plenum Press, New York, 1995).

An immunogenic composition or a vaccine according to the disclosure can be prepared in accordance with standard techniques well known to those skilled in the pharmaceutical or veterinary art. Such compositions can be administered in dosages and by techniques well known to those skilled in the medical or veterinary arts, taking into consideration such factors as the age, sex, weight, species, and condition of the particular subject, and the route of administration. The immunogenic composition or the vaccine can be administered alone, or in combination with adjuvant(s) and/or with other antigen(s). The other antigen(s) can be a Leishmania antigen. In one embodiment, the Leishmania antigen is the A2 antigen, such as the A2 antigen from *L. infantum* (see Published PCT Patent Application No. WO 95/06729 and in particular the sequence given in SEQ ID NO:2). The other antigen(s) can be present in the composition as a protein, or as an immunological fragment thereof (for example, an epitope), or as an insert in an expression vector (for example, recombinant viral vector, recombinant plasmid, in particular the pVR1012 (Vical Inc.; Hartikka J. *et al.*, *Human Gene Therapy* 7:1205-1217, 1996)).

Any immunogenic composition, vaccine, or therapeutic composition according to the disclosure can be mixed with an adjuvant.

Polypeptide-based compositions:

In several embodiments, the polypeptide-based immunogenic compositions and vaccines according to the disclosure are formulated with (1) vitamin E, saponin (for example, Quil A™, QS21™), aluminum hydroxide, aluminum phosphate, aluminum oxide ("Vaccine Design, The subunit and adjuvant approach," *Pharmaceutical Biotechnology*, vol. 6, Edited by Micheal F. Powell and Mark J. Newman, 1995, Plenum Press New York), (2) an acrylic acid or methacrylic acid polymer, a polymer of maleic anhydride and of alkenyl derivative, (3) an immunostimulating sequence (ISS), in particular an oligodeoxyribonucleotidic sequence bearing one or more non-methylated CpG groups (Klinman D. M. *et al.*, *Proc. Natl. Acad. Sci. USA* 93:2879-2883, 1996; Published PCT Application No. WO 98/16247), (4) to formulate the immunogenic or vaccine preparation in the form of an oil-in-water emulsion, in particular the SPT emulsion described on page 147 of "Vaccine Design, The Subunit and Adjuvant Approach" edited by M. Powell and M. Newman, Plenum Press, 1995, and the emulsion MF59 described on page 183 of this same book, (5) cytokines, or (6) combinations or mixtures thereof.

The cytokines (5) that can be added to the composition, include, but are not limited to, GM-CSF (granulocyte-macrophage colony stimulating factor) or cytokines inducing Th1 (for example, IL-12). All these cytokines can be added to the composition as a protein or as a vector encoding this cytokine protein. In one embodiment, the cytokines are from canine origin, for example, canine GM-CSF, for which a gene sequence has been deposited at the GenBank database (Accession No. S49738). This sequence can be used to create the vector in a manner similar to what was made in the Published PCT Patent Application No. WO 00/77210.

In one specific, non-limiting example the adjuvant contains two or more of an emulsifier, a micelle-forming agent, and an oil. Suitable emulsifiers, micelle-forming agents, and oils are detailed in U.S. Patent Nos. 5, 585,103; 5,709,860; 5,270,202; and 5,695,770, all of which are incorporated by reference. An emulsifier is any molecule that allows the components of the emulsion to remain as a stable emulsion. Such emulsifiers include polysorbate 80 (Sorbitan-mono-9-octadecenoate-poly(oxy-1,2-ethanediyl); manufactured by ICI Americas, Wilmington, Del.), polysorbate 20, polysorbate 21, polysorbate 40, polysorbate 60, polysorbate 61, polysorbate 85, dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate, TEEPOL HB7 ™, and SPAN 80 ™ SPAN 85 ™, ethoxylated fatty alcohols, ethoxylated fatty acids, ethoxylated castor oil (hydrogenated or not). In one embodiment, these emulsifiers are provided in an amount of approximately 0.05 to approximately 0.5%. In another embodiment, these emulsifiers are provided in an amount of approximately 0.2%. A micelle forming agent is an agent which is able to stabilize the emulsion formed with the other components such that a micelle-like structure is formed.

Examples of such agents include polymer surfactants described by BASF Wyandotte publications, for example, Schmolka, *J. Am. Oil. Chem. Soc.* 54:110, 1977, and Hunter *et al.*, *J. Immunol.* 129:1244, 1981, PLURONIC™ L62LF, L101, L121, and L64, PEG1000, and TETRONIC™ 1501, 150R1, 701, 901, 1301, and 130R1. The chemical structures of such agents are well known in the art. In one embodiment, the agent is chosen to have a hydrophile-lipophile balance

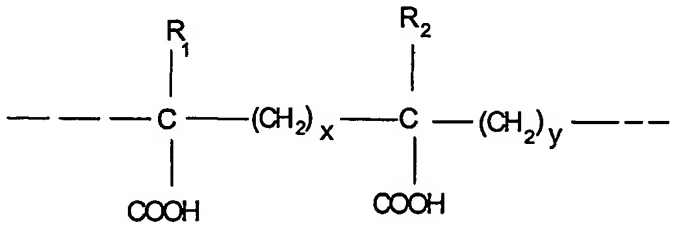
(HLB) of between about 0 and about 2, as defined by Hunter and Bennett, *J. Immun.* 133:3167, 1984. In one embodiment, the agent can be provided in an effective amount, for example between about 0.5 and about 10%. In another embodiment, the agent can be provided in an effective amount, for example between about 1.25 and about 5%.

In one embodiment, the oil included in the composition is chosen to promote the retention of the antigen in oil-in-water emulsion, for instance, to provide a vehicle for the desired antigen. In another embodiment, the oil has a melting temperature of less than about 65° C such that emulsion is formed either at room temperature (about 20° C to about 25° C), or once the temperature of the emulsion is brought down to room temperature.

The oil-in-water emulsion (4) can be based in particular on light liquid paraffin oil (European Pharmacopea type); isoprenoid oil such as squalane, squalene, EICOSANE™ or tetratetracontane; oil resulting from the oligomerization of alkenes, in particular of isobutene or decene; esters of acids or of alcohols containing a linear alkyl group, more particularly plant oils, ethyl oleate, propylene glycol di(caprylate/caprate), glyceryl tri(caprylate/caprate) or propylene glycol dioleate; esters of branched fatty acids or alcohols, in particular isostearic acid esters. The oil is used in combination with emulsifiers to form the emulsion. In several embodiments, the emulsifiers are nonionic surfactants, in particular esters of sorbitan, mannide (for example, anhydromannitol oleate), glycerol, polyglycerol, propylene glycol, and oleic, isostearic, ricinoleic, or hydroxystearic acid, which are optionally ethoxylated, and polyoxypropylene-polyoxyethylene copolymer blocks, in particular the Pluronic® products, especially L121. In one specific, non-limiting example, the oil is provided in an amount between about 1 and about 60%. In another specific, non-limiting example, the oil is provided in an amount between about 5 and about 30%. In one embodiment, the adjuvant is a mixture of emulsifiers, micelle-forming agent, and oil available under the name Provax® (IDEC Pharmaceuticals, San Diego, CA).

The acrylic acid or methacrylic acid polymers (2) can be cross-linked in particular with polyalkenyl ethers of sugars or of polyalcohols. These compounds are known under the term "carbomer" (*Pharmeuropa*, Vol. 8, No. 2, June 1996). A person skilled in the art may also refer to U.S. Patent No. 2,909,462 (incorporated by reference) describing such acrylic polymers cross-linked with a polyhydroxylated compound containing at least 3 hydroxyl groups. In one embodiment, a polyhydroxylated compound contains not more than 8 hydroxyl groups. In another embodiment, the hydrogen atoms of at least 3 hydroxyls are replaced with unsaturated aliphatic radicals containing at least 2 carbon atoms. In other embodiments, radicals contain from about 2 to about 4 carbon atoms, for example, vinyls, allyls, and other ethylenically unsaturated groups. The unsaturated radicals can themselves contain other substituents, such as methyl. The products sold under the name Carbopol® (Noveon Inc., Ohio, USA) are particularly suitable. They are cross-linked with an allyl sucrose or with allylpentaerythritol. Among these, mention may be made of the products Carbopol® 974P, 934P, and 971P.

The copolymers of maleic anhydride and of an alkenyl derivative, such as the EMA® products (Monsanto) which are copolymers of maleic anhydride and of ethylene, may be linear or cross-linked, for example cross-linked with divinyl ether. Reference may be made to J. Fields *et al.*, *Nature* 186:778-780, 1960 (incorporated by reference). In one embodiment, the acrylic acid or methacrylic acid polymers and the EMA® products are formed from units based on the following formula:



in which:

- R_1 and R_2, which may be identical or different, represent H or CH_3
- x = 0 or 1, in one embodiment, x = 1
- y = 1 or 2, with x + y = 2.

For the EMA® products, x = 0 and y = 2. For the carbomers, x = y = 1.

In one embodiment, the dissolution of these polymers in water leads to an acid solution, which is neutralized to physiological pH, in order to give to the subject the adjuvant solution into which the immunogenic composition or the vaccine itself is incorporated. The carboxyl groups of the polymer are then partly in COO^- form.

In one embodiment, a solution of adjuvant, especially of carbomer, is prepared in distilled water. In another embodiment, a solution of adjuvant, especially of carbomer, is prepared in the presence of sodium chloride, the solution obtained being at acidic pH. In another embodiment, this stock solution is diluted by adding it to the desired quantity (for obtaining the desired final concentration), or a substantial part thereof, of water charged with NaCl. In yet another embodiment, stock solution is diluted by adding it to the desired quantity of physiological saline (NaCl 9 g/l) all at once in several portions with concomitant or subsequent neutralization (pH 7.3 to 7.4). In one embodiment, the stock solution is neutralized with NaOH. This solution at physiological pH is used as it is for mixing with the immunogenic composition or with the vaccine, which may be especially stored in freeze-dried, liquid or frozen form.

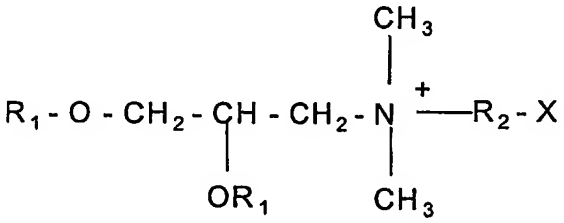
In one embodiment, the polymer concentration in the final vaccine composition is from about 0.01 to about 1.5% W/V. In another embodiment, the final vaccine composition is from about 0.05 to about 1% W/V. In yet another embodiment, the final vaccine composition is from about 0.1 to about 0.4% W/V.

Lipids have been identified as agents capable of stimulating the immune response for various antigens. For example, as described in U.S. Patent No. 5,662,907, palmitic acid residues can be attached to the alpha and epsilon amino groups of a lysine residue and then linked (for example, via one or more linking residues, such as glycine, glycine-glycine, serine, serine-serine, or the like) to an immunogenic peptide. The lipidated peptide can then be injected directly in a micellar form, incorporated in a liposome, or emulsified in an adjuvant. As another example, *E. coli* lipoproteins, such as tripalmitoyl-S-glycerylcysteinylseryl-serine, can be used.

To extend the time during which the peptide or protein is available to stimulate a response, the peptide or protein can be provided as an implant, an oily injection, or as a particulate system. The particulate system can be a microparticle, a microcapsule, a microsphere, a nanocapsule, or similar particle. (see, for example, Banja, *supra)*. A particulate excipient based on a synthetic polymer has been shown to act as an adjuvant to enhance the immune response, in addition to providing a controlled release.

Plasmid-based compositions:

In one embodiment, the plasmid-based compositions is formulated with cationic lipids, in particular with cationic lipids containing a quaternary ammonium salt having the following formula:



in which R1 is a saturated or unsaturated linear aliphatic radical from 12 to 18 carbon atoms, R2 is another aliphatic radical comprising from 2 to 3 carbon atoms, and X is an hydroxyl or amine group.

In one embodiment, DMRIE (N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-1-propanammonium; Published PCT Application No. WO 96/34109) is the cationic lipid. In another embodiment, the cationic lipid is in association with a neutral lipid, for example DOPE (dioleoyl-phosphatidyl-ethanolamine; Behr J. P., *Bioconjugate Chemistry* 5:382-389, 1994), in order to form the DMRIE-DOPE. In yet another embodiment, the mixture is made extemporaneously about 10 minutes to about 60 minutes before administration. In another embodiment, the mixture is made extemporaneously about 30 minutes before administration. In one embodiment, the molar ratio DMRIE/DOPE is from about 95/5 to about 5/95. In another embodiment, the molar ratio DMRIE/DOPE is about 1/1. In one embodiment, the weight ratio plasmid/DMRIE or DMRIE-DOPE adjuvant is from about 50/1 to about 1/10. In another embodiment, the weight ratio plasmid/DMRIE or DMRIE-DOPE adjuvant is from about 10/1 to about 1/5. In yet another embodiment, the weight ratio plasmid/DMRIE or DMRIE-DOPE adjuvant is from about 1/1 to about 1/2.

In one embodiment, a cytokine or non-methylated CpG groups is added to the composition, as described above for polypeptide-based compositions. The addition can be done advantageously by a plasmid encoding the cytokine.

Viral vector-based composition:

The recombinant viral vector-based composition can be supplemented with fMLP (N-formyl-methionyl-leucyl-phenylalanine; U.S. Patent No. 6,017,537) and/or acrylic acid or methacrylic acid polymer adjuvant as described above for polypeptide-based compositions. They can also be formulated with emulsions as described above.

In one embodiment, cytokines, non-methylated CpG groups, or emulsions are added to the composition as described above for polypeptide-based compositions. The addition can be done advantageously by a viral vector encoding said cytokine.

The immunogenic compositions and vaccines according to the disclosure are conserved and stored either in formulated form at 5°C, or in lyophilized form. In one embodiment, the immunogenic compositions and vaccines according to the disclosure are conserved and stored either in formulated form at 5°C, or in lyophilized form with a stabilizer. Freeze-drying can be done according to well-known standard freeze-drying procedures. The pharmaceutically acceptable stabilizers may be SPGA (sucrose phosphate glutamate albumin) (Bovarnik *et al., J. Bacteriology* 59:509, 1950), carbohydrates (for example, sorbitol, mannitol, lactose, sucrose, glucose, dextran, trehalose), sodium glutamate (Tsvetkov T. *et al., Cryobiology* 20(3):318-23, 1983 ; Israeli E. *et al., Cryobiology* 30(5):519-23, 1993), proteins such as peptone, albumin, or casein, protein containing agents such as skimmed milk (Mills CK *et al., Cryobiology* 25(2):148-52, 1988; Wolff E. *et al., Cryobiology* 27(5):569-75, 1990), and buffers (for example, phosphate buffer, alkaline metal phosphate buffer). An adjuvant may be used to make soluble the freeze-dried preparations.

Methods of Immunization

The present disclosure provides methods for inducing an immune response to a Lutzomyia sand fly polypeptide in a subject. The present disclosure provides further methods for inhibiting or preventing leishmaniasis in a subject.

These methods include the administration of at least one immunogenic composition or vaccine according to the disclosure.

An immunogenic composition or a vaccine according to the disclosure can be prepared in accordance with standard techniques well known to those skilled in the pharmaceutical or veterinary art. Such compositions can be administered in dosages and by techniques well known to those skilled in the medical or veterinary arts, taking into consideration such factors as the age, sex, weight, species, and condition of the particular subject, and the route of administration.

If more than one administration is required, they can be administered concurrently (for example, different compositions given during the same period of time via the same or different routes, or a same composition given in the same period of time via different routes), or sequentially

(for example, the same or different compositions given at least two times via the same or different routes). In one embodiment, the delay between two sequential administrations is from about 1 week to about 6 months. In another embodiment, the delay is from about 3 weeks to about 6 weeks. In yet another embodiment, the delay is from about 4 weeks. Following vaccination, annual boost administrations may be done. Advantageously, in a prime-boost vaccination schedule, at least one prime-administration can be done with a composition containing a plasmid according to the disclosure, following by at least one booster administration done with a composition containing a recombinant viral vector according to the disclosure, on the condition that a same *Lu. longipalpis* salivary polypeptide is present twice, coded by the plasmid and by the viral vector. Alternatively, the booster administration can be done with a composition containing a polypeptide according to the disclosure, on the condition that a same *Lu. longipalpis* salivary polypeptide is present twice, coded by the prime-administration plasmid and in the booster polypeptide-based composition.

In such compositions the antigen(s) may be in admixture with a suitable vehicle or excipient such as sterile water, physiological saline, glucose, or the like. The compositions can contain auxiliary substances such as wetting or emulsifying agents, pH buffering agents, adjuvants, gelling, or viscosity enhancing additives, preservatives, flavoring agents, colors, and the like, depending upon the route of administration and the preparation desired. Standard texts, such as Remington's Pharmaceutical Science, 17th edition, 1985, incorporated herein by reference, may be consulted to prepare suitable preparations, without undue experimentation. The compositions can also be lyophilized.

Suitable dosages can also be based upon the examples below. For polypeptide-based compositions, the route of administration can be ID, IM, SC, intravenous, oral, nasal, or anal. This administration can be made with a syringe and a needle or with a needle-less apparatus like, for example, Biojector™ (Bioject, Oregon, USA). In several embodiments, polypeptide dosages can be from about 1 to 250 μg/ml, from about 15 to about 150 μg/dose, or from about 20 to about 100 μg/dose. In another embodiment, using a needle-less apparatus the volume of a dose can be between about 0.1 ml and about 0.5 ml. In yet another embodiment, using a needle-less apparatus the volume of a dose can be about 0.25 ml. Administration with multiple points of injection is preferred. In one embodiment, for conventional injection with a syringe and a needle, the volumes are from about 0.1 to about 2 ml. In another embodiment, for conventional injection with a syringe and a needle, the volumes are from about 0.5 to about 1 ml.

For plasmid-based compositions, the route of administration can be ID, IM, SC, intravenous, oral, nasal, or anal. This administration can be made with a syringe and a needle or with a needle-less apparatus like, for example, Biojector™. The dosage is from about 50 μg to about 500 μg per plasmid. When DMRIE-DOPE is added, about 100 μg per plasmid is preferred. In one embodiment, when canine GM-CSF or other cytokine is used, the plasmid encoding this protein is present at a dosage from about 200 μg to about 500 μg. In another embodiment, the plasmid encoding this protein is present at a dosage of about 200 μg. In one embodiment, using a needle-less apparatus, the volume of a dose can be between about 0.1 ml and about 0.5 ml. In another embodiment, the volume

of a dose can be about 0.25 ml. In yet another embodiment, administration is performed using multiple points of injection. In one embodiment, for conventional injection with a syringe and a needle, the volumes are from about 0.1 to about 2 ml. In another embodiment, the volumes are from about 0.5 to about 1 ml. The dosage are the same than mentioned above.

For recombinant viral vector-based compositions, the route of administration can be ID, IM, SC, intravenous, oral, nasal, or anal. This administration can be made with a syringe and a needle or with a needle-less apparatus like, for example, Biojector™. The dosage is from about 10^3 pfu to about 10^9 pfu per recombinant poxvirus vector. In one embodiment, when the vector is a canarypox virus, the dosage is from about 10^5 pfu to about 10^9 pfu. In another embodiment, the dosage is from about 10^6 pfu to about 10^8 pfu. In one embodiment, the volume of needle-less apparatus doses could be between about 0.1 ml and about 0.5 ml. In another embodiment, the volume of needle-less apparatus dose is 0.25 ml. In yet another embodiment, administration is performed using multiple points of injection. In one embodiment, for conventional injection with a syringe and a needle, the volumes are from about 0.1 to about 2 ml. In another embodiment, the volumes are from about 0.5 to about 1 ml. The dosages are the same as mentioned above. In one embodiment, when a syringe with a needle is used, the injection is IM.

Advantageously for the prime boost administration regimen, the prime-administration is made with a plasmid-based composition and the boost administration is made with a recombinant viral vector-based composition. In one embodiment, the boost administration is made with a canarypox vector. Both priming and boosting administrations include vectors encoding at least one identical *Lu. longipalpis* salivary antigens, and optionally Leishmania A2 antigens. The dosage of plasmids and recombinant viral vectors are the same as above. Optionally, the boost administration can be done with a polypeptide-based composition. In this case, the dosage of polypeptide is from about 1 to about 250 μg/ml, from about 15 to about 150 μg/dose, or from about 20 to about 100 μg/dose.

Immunization by nucleic acid constructs is well known in the art and taught, for example, in U.S. Patent No. 5,643,578 (which describes methods of immunizing vertebrates by introducing DNA encoding a desired antigen to elicit a cell-mediated or a humoral response) and U.S. Patent No. 5,593,972 and U.S. Patent No. 5,817,637 (which describe operably linking a nucleic acid sequence encoding an antigen to regulatory sequences enabling expression). U.S. Patent No. 5,880,103 describes several methods of delivery of nucleic acids encoding immunogenic peptides or other antigens to an organism. The methods include liposomal delivery of the nucleic acids (or of the synthetic peptides themselves), and immune-stimulating constructs, or ISCOMS™, negatively charged cage-like structures of 30-40 nm in size formed spontaneously on mixing cholesterol and Quil A™ (saponin). Protective immunity has been generated in a variety of experimental models of infection, including toxoplasmosis and Epstein-Barr virus-induced tumors, using ISCOMS™ as the delivery vehicle for antigens (Mowat and Donachie, *Immunol. Today* 12:383, 1991). Doses of antigen as low as 1 μg encapsulated in ISCOMS™ have been found to produce class I mediated CTL responses (Takahashi *et al.*, *Nature* 344:873, 1990).

In another approach to using nucleic acids for immunization, a *Lu. longipalpis* polypeptide, or an immunogenic fragment thereof, can also be expressed by attenuated viral hosts or vectors or bacterial vectors. Recombinant vaccinia virus, adeno-associated virus (AAV), herpes virus, retrovirus, or other viral vectors can be used to express the peptide or protein, thereby eliciting a CTL response. For example, vaccinia vectors and methods useful in immunization protocols are described in U.S. Patent No. 4,722,848. BCG (Bacillus Calmette Guerin) provides another vector for expression of the peptides (see Stover, *Nature* 351:456-460, 1991).

In one embodiment, a nucleic acid encoding a *Lu. longipalpis* polypeptide, or an immunogenic fragment thereof, is introduced directly into cells. For example, the nucleic acid may be loaded onto gold microspheres by standard methods and introduced into the skin by a device such as Bio-Rad's Helios™ Gene Gun. A needless injector can also be utilized, such as a Bioinjector2000™. The nucleic acids can be "naked," consisting of plasmids under control of a strong promoter. Typically, the DNA is injected into muscle, although it can also be injected directly into other sites. Exemplary dosages for injection are around 0.5 μg/kg to about 50 mg/kg, and typically are about 0.005 mg/kg to about 5 mg/kg (see, for example, U.S. Patent No. 5,589,466). In one embodiment, a prime-boost strategy for immunization is utilized. Thus, in one embodiment, a nucleic acid encoding a *Lu. longipalpis* polypeptide is administered to the subject, followed by immunization with an attenuated or inactivated form of Leishmania.

The immunogenic compositions and the vaccines disclosed herein can be administered for preventative and therapeutic treatments. In therapeutic applications, compositions are administered to a subject suffering from a disease, such as *Leishmaniasis*, in a therapeutically effective amount, which is an amount sufficient to cure or at least partially arrest the disease or a sign or symptom of the disease. Amounts effective for this use will depend upon the severity of the disease and the general state of the subject's health. An effective amount of the compound is that which provides either subjective relief of a symptom(s) or an objectively identifiable improvement as noted by the clinician or other qualified observer.

Single or multiple administrations of the compositions are administered depending on the dosage and frequency as required and tolerated by the subject. In one embodiment, the dosage is administered once as a bolus, but in another embodiment can be applied periodically until a therapeutic result is achieved. Generally, the dose is sufficient to treat or ameliorate symptoms or signs of disease without producing unacceptable toxicity to the subject.

As noted above, the dosage of the composition varies depending on the weight, age, sex, and method of administration. The dosage can also be adjusted by the individual physician as called for based on the particular circumstances. The compositions can be administered conventionally as vaccines containing the active composition as a predetermined quantity of active material calculated to produce the desired therapeutic or immunologic effect in association with the required pharmaceutically acceptable carrier or diluent (for instance, carrier or vehicle). For example, about 50 μg of a DNA construct vaccine of the present disclosure can be injected intradermally three times

at two week intervals to produce the desired therapeutic or immunologic effect. In another embodiment, a about 1 mg/Kg dosage of a protein vaccine of the present disclosure can be injected intradermally three times at two week intervals to produce the desired therapeutic or immunologic effect.

A vaccine is provided herein that includes a *Lu. longipalpis* polypeptide or polynucleotide. Administration of the vaccine to a subject, such as a human or veterinary subject, results in resistance to infection with *Leishamania*. In one embodiment, the subject is a human subject. In another embodiment, the subject is a canine subject, such as a dog.

Methods and Kits for the Diagnosis of *Leishmania* Infection

It is disclosed herein that individuals who experience an anti-*Leishmania* DTH response conversion also have an increase in antibodies against *Lu. Longipalpis* polypeptide salivary proteins. Thus, the presence or absence of antibodies to *Lu. Longipalpis* polypeptide salivary proteins can be used to ascertain if a subject has a *Leishmania* infection.

A method is disclosed herein for diagnosing infection with *Leishmana* by detecting the presence of antibodies that specifically bind one or more polypeptides having an amino acid sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, or a polypeptide at least 80%, at least 90%, at least 95%, or at least 99% homologous to one of these polypeptides, a conservative variant, a homolog or an immunogenic fragment of one of these polypeptides. The method can utilize a single *Lu. Longipalpis* polypeptide or a combination of these polypeptides. In certain examples, the method of diagnosis detects antibodies that specifically bind at least 3, 6, or 10 of these polypeptides, or immunogenic fragments thereof.

In one embodiment, one or more *Lu. Longipalpis* polypeptide can be bound to a solid substrate. For example, the *Lu. Longipalpis* polypeptide having an amino acid sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67 can be bound to the substrate. One of more of these polypeptides can be bound to the substrate, for example at least 3, 6, or 10 of these polypeptides, or an immunogenic fragment thereof. In one example, one or more polypeptides having a sequence set forth as one of SEQ ID NO: 3, SEQ ID NO: 11, SEQ ID NO: 19, SEQ ID NO: 29, SEQ ID NO: 55, or SEQ ID NO: 59 can be bound to the substrate. In another example, one or more *Lu. Longipalpis* a polypeptides having a sequence set forth as one of SEQ ID NO: 1, SEQ ID NO: 23, or SEQ ID NO: 39 can be bound to the substrate. In one specific, non-

limiting example, at least six *Lu. Longipalpis* polypeptides are bound to a solid substrate, wherein each of the polypeptides comprises an amino acid sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 11, SEQ ID NO: 19, SEQ ID NO: 29, SEQ ID NO: 55, or SEQ ID NO: 59, or an immunogenic fragment thereof. In another specific, non-limiting example, at least three *Lu. Longipalpis* polypeptides are bound to a solid substrate, wherein each of the polypeptides comprises an amino acid sequence as set forth as SEQ ID NO: 1, SEQ ID NO: 23, or SEQ ID NO: 39, or an immunogenic fragment thereof.

In one embodiment, two or more (for example at least 3, 6, or 10) *Lu. Longipalpis* polypeptides (or immunogenic fragments thereof) are applied to a solid substrate, for example as a series of "dots," such as in a "dot blot" assay. In another embodiment, two or more *Lu. Longipalpis* polypeptides are applied to a substrate such as in a linear array. In a further embodiment, *Lu. Longipalpis* polypeptides are applied to a membrane in a two-dimensional array. In this manner, the presence of antibodies to more than one *Lu. Longipalpis* polypeptide is assessed. Each *Lu. Longipalpis* polypeptide can be applied directly to the surface of a membrane in a single location or in a combination of locations.

The solid substrate can be a polystyrene bead, a membrane, a chip or a plate. A plastic or glass substrate can be utilized. In other embodiments, a membrane is utilized that is composed of porous materials such as nylon, nitrocellulose, cellulose acetate, glass fibers, and other porous polymers. The surface of a solid support may be activated by chemical processes that cause covalent linkage of polypeptide to the support. However, any other suitable method may be used for immobilizing a polypeptide to a solid support including, without limitation, ionic interactions, hydrophobic interactions, covalent interactions and the like. Once the polypeptide is applied to the substrate, the substrate can be contacted with a substance, such as protein-containing solution, which non-specifically saturates the binding sites thereon. Specific, non-limiting examples of a protein-containing solution include a solution made from powdered milk or serum albumin, such as bovine serum albumin.

A specimen (for example, sera, blood, plasma, urine, semen, saliva, sputum, lacrimal fluid, lymph fluid) is then added to the substrate, and the combined specimen and substrate are incubated for a sufficient time to allow specific binding. Specific binding of antibodies to the *Lu. Longipalpis* polypeptides disclosed herein, are then detected using any means known to one of skill in the art. In one embodiment, a labeled secondary antibody is used to detect the antibodies that specifically bind the *Lu. Longipalpis* polypeptides. The label can be a radiolabel (for example, ^{125}I), an enzymatic label (for example, alkaline phosphatase or horseradish peroxidase), or a fluorescent label (for example, fluoroscein isothiocyanate). Detection systems for these labels are known to one of skill in the art. Binding of the specimen, or a component of the specimen, to the *Lu. Longipalpis* polypeptide, as indicated by the presence of the marker, indicates infection with *Leishmania.*

In another embodiment, the specimen is adsorbed onto a solid substrate containing binding sites for polypeptides, such as antibody molecules. In one embodiment, the solid substrate is a polystyrene bead, a chip, a membrane or a plate. The substrate is thereafter contacted with a

substance, such as a protein-containing solution that non-specifically saturates the binding sites thereon. The substrate is then washed with a buffer. A solution of one or more *Lu. Longipalpis* polypeptides is then added to the bound specimens. In one embodiment, the *Lu. Longipalpis* polypeptide is directly labeled. The labeling of the *Lu. Longipalpis* polypeptide can be brought about by use of any marker, such as by incorporation of a radioactive isotope or group, or by coupling this component to an enzyme, a dyestuff, for example a chromophoric moiety or a fluorescent group. The enzymes of use are those which can be colorimetrically, spectrophotometrically, or fluorimetrically determined. Non-limiting examples of enzymes for use in the present invention include enzymes from the group of oxidoreductases, such as catalase, peroxidase, glucose oxidase, beta-glucuronidase, beta-D-glucosidase, beta-D-galactosidase, urease and galactose oxidase. After the labeled *Lu. Longipalpis* polypeptide is incubated with the solid substrate, any unbound labeled *Lu. Longipalpis* polypeptide is removed by washing. Bound labeled *Lu. Longipalpis* polypeptide is then detected by an appropriate assay. Binding of the labeled *Lu. Longipalpis* polypeptide to the specimen, or to a component of the specimen, is indicative of infection with *Leishmania*.

In general, the incubation steps utilized in carrying out the procedures can be performed in a known manner, such as by incubating at temperatures between about 4° C and about 25° C, for about 30 minutes to about 48 hours. Washings can be included with an aqueous solution such as a buffer, wherein the buffer is from about pH 6 to about pH 8, such as by using an isotonic saline solution of a pH of about 7.

Competitive binding assays are also of use in detecting infection with *Leishmania*. One of skill in the art, given the *Lu. Longipalpis* polypeptides disclosed herein, will readily be able to design additional assays, such as competitive binding assays, of use in detecting *Leishmania* infection.

In another embodiment, the *Lu. Longipalpis* polypeptides disclosed herein can be included in a diagnostic test kit. For example, a diagnostic test kit for detecting a *Leishmania* infection includes a solid substrate having applied thereon one or more *Lu. Longipalpis* polypeptide disclosed herein. In other embodiments, the kit includes written instructions and/or a container including a specified amount of labeled antibodies to immunoglobulins, such as IgG or IgM, or labeled secondary antibodies that bind antibodies from a species of interest. For example labeled antibodies can be provided that specifically detect dog or human immunoglobulins. The labeled antibodies can be fluorescently labeled, enzymatically labeled, or radiolabeled. Labeled antibodies used in the above-described test kits can be packaged in either solution form, or in lyophilized forms suitable for reconstitution.

In another embodiment the test kit includes a specified amount of one or more *Lu. Longipalpis* polypeptide described herein in a container, and written instructions. In one example, the *Lu. Longipalpis* polypeptide is directly labeled. In another example, the one or more *Lu. Longipalpis* polypeptide is unlabeled. If the *Lu. Longipalpis* polypeptide is unlabeled, a container can also be included with a detection reagent that specifically binds the *Lu. Longipalpis* polypeptide, such as a labeled monoclonal antibody. The kit can also optionally include a solid substrate for binding the specimen.

The above described process and test kit for detection of antibodies to the *Lu. Longipalpis* polypeptides disclosed herein can be utilized in many applications, including, but not limited to detecting *Leishmania* infection in a subject using the methods disclosed herein. The tests and kits disclosed herein can be used to detect the efficacy of a therapeutic treatment in a subject. In yet another embodiment, the tests and kits disclosed herein can also be used to assess a primary infection with *Leishmania* or to predict recovery from *Leishmania* infection by taking a body fluid from an infected subject, for example at various times following infection, and applying the above described detection procedures.

The disclosure is illustrated by the following non-limiting Examples.

EXAMPLES

Example 1
Library Construction

Sand Flies and Preparation of salivary gland homogenate (SGH). Sand fly Lutzomyia longipalpis salivary glands were obtained from colonized sand flies at Walter Reed Army Institute and at the National Institutes of Health.

Salivary glands dissected under a dissection microscope and collected in microfuge tubes in sterile phosphate buffered saline (PBS), pH 7.0 are stored in dry ice and transferred to –70° C until use.

The salivary gland of *Lu. longipalpis* is a sac-like structure consisting of a unicellular epithelium layer surrounding a large lumen (Adler and Theodor, *Ann. Trop. Med. Parasitol.* 20:109, 1926). After a blood meal, the gland total protein content decreases to half or less from its ~1μg value (Ribeiro *et al., Insect Biochem.* 19:409-412, 1989). Accordingly, most of the protein from the fly SGH must be destined for secretion. Indeed, SDS-PAGE of SGH reveals a low complexity composition consisting of ~12 major bands varying from 10-100 kD (Valenzuela *et al., J. Exp. Med.* 194:331-42, 2001). For SDS-PAGE, Tris-glycine gels (16%), 1 mm thick, and NUPAGE 12% BIS-tris gels were used (Invitrogen, Carlsbad, CA). Gels were run with either Tris-glycine or MOPS Nupage running buffer according to the manufacturer's instructions. To estimate the molecular weight of the samples, See BlueJ markers from Invitrogen (myosin, BSA, glutamic dehydrogenase, alcohol dehydrogenase, carbonic anhydrase, myoglobin, lysozyme, aprotinin, and insulin, chain B) were used.

SGH were treated with equal parts of 2X SDS sample buffer (8% SDS in Tris-HCl buffer, 0.5M, pH 6.8, 10% glycerol and 1% bromophenol blue dye). Thirty pairs of homogenized salivary glands per lane (approximately 30μg protein) were applied when visualization of the protein bands stained with Coomassie blue was desired. For amino terminal sequencing of the salivary proteins, 40 homogenized pairs of glands were electrophoresed and transferred to polyvinylidene difluoride (PVDF) membrane using 10 mM CAPS, pH 11, 10% methanol as the transfer buffer on a Blot-

Module for the XCell II Mini-Cell (Invitrogen, Carlsbad, CA). The membrane was stained with Coomassie blue in the absence of acetic acid. Stained bands were cut from the PVDF membrane and subjected to Edman degradation using a Procise sequencer (Perkin-Elmer Corp, Foster City, CA).

Salivary Gland cDNA Library Construction. Lu. longipalpis salivary gland mRNA was isolated from 80 salivary gland pairs from adult females. The Micro-FastTrack mRNA isolation kit (Invitrogen, Carlsbad, CA) was used, yielding approximately 100 ng poly (A)+ mRNA. The PCR-based cDNA library was made following the instructions for the SMART cDNA library construction kit (Clontech, Palo Alto, CA). One hundred nanograms of *Lu. longipalpis* salivary gland mRNA was reverse transcribed to cDNA using Superscript II RNase H- reverse transcriptase (Gibco-BRL, Gaithersburg, MD) and the CDS/3' primer (Clontech, Palo Alto, CA) for 1 hour at 42° C. Second strand synthesis was performed using a PCR-based protocol by using the SMART III primer (Clontech, Palo Alto, CA) as the sense primer and the CDS/3' primer as anti-sense primer, these two primers additionally, create at the ends of the nascent cDNA SfiI A and B sites respectively. Double strand cDNA synthesis was done on a Perkin Elmer 9700 Thermal cycler (Perkin Elmer Corp., Foster City, CA) and using the Advantage Klen-Taq DNA polymerase (Clontech, Palo Alto, CA). PCR conditions were the following: 94° C for 2 minutes; 19 cycles of 94°C for 10 seconds and 68° C for 6 minutes. Double-stranded cDNA was immediately treated with proteinase K (0.8 μg/μl) for 20 minutes at 45° C and washed three times with water using Amicon filters with a 100 kDa cut off (Millipore Corp., Bedford MA). The double-stranded cDNA was then digested with Sfi I for 2 hours at 50° C (The Sfi I sites were inserted to the cDNA during the second strand synthesis using the SMART III and the CDS/3' primer). The cDNA was then fractionated using columns provided by the manufacturer (Clontech, Palo Alto, CA). Fractions containing cDNA of more than 400 base pairs (bp) were pooled, concentrated, and washed three times with water using an Amicon filter with a 100 kDa cut-off. The cDNA was concentrated to a volume of 7 μl. The concentrated cDNA was then ligated into a lambda triplex2 vector (Clontech, Palo Alto, CA), and the resulting ligation reaction was packed using the Gigapack gold III from Stratagene/Biocrest (Cedar Creek, TE) following manufacturer's specifications. The obtained library was plated by infecting log phase XL1-blue cells (Clontech, Palo Alto, CA) and the amount of recombinants was determined by PCR using vector primers flanking the inserted cDNA and visualized on a 1.1 % agarose gel with ethidium bromide (1.5 μg/ml)

Massive Sequencing of Lu. longipalpis Salivary Gland cDNA Library.

Lu. longipalpis salivary gland cDNA library was plated to approximately 200 plaques per plate (150 mm Petri dish). The plaques were randomly picked and transferred to a 96 well polypropylene plate containing 100 μl of water per well. The plate was covered and placed on a gyrator shaker for 1 hour at room temperature. Four microliters of a phage sample was used as a template for a PCR reaction to amplify random cDNAs. The primers used for this reaction were sequences from the triplex2 vector, the primers were named PT2F1 (5'- AAGTACTCT AGCAAT TGTGAGC- 3') (SEQ ID NO:71) which is positioned upstream of the cDNA of interest (5' end), and PT2R1 (5'- CTCTTCGCTATTACGCCAGCT G- 3') (SEQ ID NO:72) which is positioned downstream of the

cDNA of interest (3' end). Platinum Taq polymerase (Gibco-BRL, Gaithersburg, MD) was used for these reactions. Amplification conditions were the following: 1 hold of 75° C for 3 minutes, 1 hold of 94° C for 3 minutes and 34 cycles of 94° C for 30 seconds, 49° C for 30 seconds and 72° C for 1 minute and 20 seconds. Amplified products were visualized on a 1.1% agarose gel with ethidium bromide. Clean PCR was used as a template for a cycle sequencing reaction using the DTCS labeling kit from Beckman Coulter Inc. (Fullerton, CA). The primer used for sequencing (PT2F3) (5'-TCTCGGGAAGCGCGCCATTGTGTT - 3') (SEQ ID NO:73) is upstream of the inserted cDNA and downstream of the primer PT2F1. Sequencing reaction was performed on a Perkin Elmer 9700 thermacycler. Conditions were 75° C for 2 minutes, 94° C for 4 minutes, and 30 cycles of 96° C for 20 seconds, 50° C for 20 seconds and 60° C for 4 minutes.

After cycle sequencing the samples, a cleaning step was done using the multi-screen 96 well plate cleaning system from Millipore (Bedford, MA). The 96 well multi-screening plate was prepared by adding a fixed amount (according to the manufacturer's specifications) of Sephadex-50 (Amersham Pharmacia Biotech, Piscataway, NJ) and 300 µl of deionized water. After 1 hour of incubation at room temperature, the water was removed from the multi screen plate by centrifugation at 750 g for 5 minutes. After the Sephadex in the multi-screen plate was partially dried, the whole cycle sequencing reaction was added to the center of each well, centrifuged at 750 g for 5 minutes and the clean sample was collected on a sequencing microtiter plate (Beckman Coulter, Fullerton, CA). The plate was then dried on Speed-Vac SC 110 model with a microtiter plate holder (Savant Instruments Inc, Holbrook, NY). The dried samples were immediately resuspended with 25 µl of deionized ultrapure formamide (J.T. Baker, Phillipsburg, NJ), and one drop of mineral oil was added to the top of each sample. Samples were sequenced immediately on a CEQ 2000 DNA sequencing instrument (Beckman Coulter Inc., Fullerton, CA) or stored at -30° C. The entire cDNA of selected genes was fully sequenced using custom primers using a CEQ 2000 DNA sequencing instrument (Beckman Coulter Inc., Fullerton, CA) as described above.

DNA Vaccine Construction and Description of the VR1020 Vector. The genes coding for the predicted secreted proteins were amplified from *Lu. longipalpis* specific cDNA by PCR using Platinum *Taq* polymerase (GIBCO BRL, Gaithersburg, MD) and specific primers carrying the Predicted N-terminus (Forward primer); and the stop codon (Reverse primer) of the selected cDNA.

The PCR product was immediately cloned into the custom made VR-2001-TOPO (derived fromVR1020 vector) cloning vector following manufacturers specifications (Invitrogen, Carlsbad, CA). The ligation mixture was used to transform TOP10 cells (Invitrogen, Carlsbad, CA) and the cells were incubated overnight at 37° C. Eight colonies were picked and mixed with 10 µl of sterile water. Five microliters of each sample were transferred to Luria broth (LB) with ampicillin (100 µg/ml) and grown at 37° C. The other 5 µl were used as a template for a PCR reaction using two vector-specific primers from the PCRII vector to confirm the presence of the insert and for sequencing analysis. After visualization of the PCR product on a 1.1% agarose gel, the eight PCR products were completely sequenced as described above using a CEQ2000 DNA sequencing

instrument (Beckman Coulter). Cells containing the plasmid carrying the selected *Lu. longipalpis* gene were grown overnight at 37° C on Luria broth with ampicillin (100 μg/ml), and plasmid isolation was performed using the Wizard Miniprep kit (Promega, Madison, WI). The VR-2001-TOPO (a variant of the VR1020 plasmid from Vical) plasmid contains a kanamycin resistance gene, the human cytomegalovirus promoter, and the tissue plasminogen activator signal peptide upstream of the TOPO TA cloning site. The sample that contained the sequence from the start codon to the stop codon in the right orientation and in the correct open-reading-frame following the nucleotide sequence encoding the tissue plasminogen activator signal peptide was chosen.

Plasmids were transformed into the TOP-10 strain of *E. coli* (Invitrogen, Carlsbad, CA) according to the manufacturer's instructions. The transformed bacteria were grown in LB medium and the plasmid was subsequently purified using the commercial plasmid purification kit Megaprep (Qiagen, Valencia, CA). Each plasmid was named according to the name of the polypeptide. Thus pLJL34 is a plasmid encoding LJL34, and pLJM11 is a plasmid encoding LJM11 polypeptide, etc.

Study population. Sera used in the study using human subjects were obtained from an epidemiologic survey of visceral leishmaniasis (VL) in children less than 7 years of age in an endemic region of São Luiz, Maranhão State, in northeastern Brazil. During this prospective study, anti-*Leishmania* DTH and serology were performed twice a year during 1997 and 1998. Only children who had neither VL, a positive serology, nor DTH on the first survey were included in the study. None of the individuals in the data set had the disease, and all had negative responses to leishmanial antigen during the preceding 6-month period. Positivity in the anti-leishmanial tests reported here indicates a recent conversion determined by a sensitive and specific ELISA (Barral *et al., Am J Trop Med Hyg* 62:740–5, 200) and/or DTH test (Barral *et al., ibid*). To determine the cut-off value for IgG anti-*Lu. longipalpis* in ELISA assays, sera were obtained from children in the same age range from a nonendemic area. Assuming that recent seroconversion represents infection and that a positive DTH response is a marker of protection against leishmaniasis in subclinical cases, we classified children in two groups according to their anti-*Leishmania* responses: Group I, positive serology ($S^- \rightarrow S^+$) (n =15) and Group II, positive DTH ($DTH^- \rightarrow DTH^+$) (n = 15).

Anti-sand fly saliva serology. Anti-sand fly saliva serology ELISA was performed as previously described (Barral *et al., ibid*). Sera IgG subclasses were determined using anti-human IgG1, IgG3, or IgG4 alkaline-phosphatase conjugates (Sigma-Aldrich, St. Louis, MO). To determine IgE levels, sera were previously absorbed using Rheumatoid Factor. Anti-human IgE (Sigma-Aldrich, St. Louis, MO) was used in the ELISA.

Western blots. Western blots of salivary gland antigens were performed as previously described (Barral *et al., ibid*).

Statistical analysis (human studies). The non-parametric paired Wilcoxon test was used to compare levels of anti-*Lu. longipalpis* saliva antibodies in the same children at time 0 (beginning of survey) and after 6 months. P value < 0.05 was established as the significance level. Graph Pad Prism software (San Diego, CA) was used to perform the statistical tests.

Example 2

DNA and Predicted Protein Sequence Analysis.

DNA data derived from the mass sequencing project were analyzed by an in-house program written in VisualBASIC (Microsoft). This program removed vector and primer sequences from the raw sequence. Stripped sequences were compared to the NCBI non-redundant protein database using the program BlastX using the BLOSUM-62 matrix (Altschul *et al.*, *Nucleic Acids Research* 25:3389, 1997). DNA sequences were clustered by blasting the database against itself with a preselected threshold cutoff, usually $1e^{-10}$ (BlastN program) (Altschul *et al.*, *Nucleic Acids Research* 25:3389, 1997). Sequences from the same cluster were aligned using ClustalX (Jeanmougin *et al.*, *Trends Biochem. Sci.* 23:403, 1998). To find the cDNA sequences corresponding to the amino acid sequence obtained by Edman degradation of the proteins transferred to PVDF membranes from SDS-PAGE gels, a search program was written that checked these amino acid sequences against the three possible protein translations of each cDNA sequence obtained in the mass sequencing project. This was written using the same approach used in the BLOCKS (Henikoff *et al.*, *Bioinformatics* 15:471, 1999) or Prosite (Bairoch, *Nucleic Acids Res.* 19 (Suppl.):2241,1991) programs. Protein translations of the full-length clones were further processed to identify the predicted signal peptides using the Signal P program (Nielsen *et al.*, *Protein Eng.* 10:1, 1997), available online. Predicted signal peptide cleaved sites were compared to the N-terminus sequence obtained from Edman degradation of *Phlebotomus* salivary proteins. Estimation of isoelectric point and molecular weight of translated protein was performed using the DNA STAR program (DNASTAR). Full-length translated protein sequence information was compared with the non-redundant protein database of NCBI using the BLAST-P program (Altschul *et al.*, *Nucleic Acids Research* 25:3389, 1997) and searched for motifs by submitting each sequence to the electronic database.

To characterize the primary structure of the main proteins of *Lu. longipalpis* SGH, SDS-PAGE gels were transferred to PVDF membranes, and the amino terminal sequence of each cut band by Edman degradation were estimated.

In addition, the following values were ascertained:

Table 1
Protein Characteristics

Polypeptide name	Position of cleavage site	Molecular Weight (MW) of Unprocessed Protein	pI of Unprocessed Protein	Molecular Weight of Processed Protein	pI of Processed Protein
LJL34	19	31	9.14	28.9	9.1
LJL18	19	18.7	6.42	16.4	6.1
LJS193	20	34.5	6.59	32.2	6.3
LJS201	23	11.2	4.89	8.7	4.8
LJL13	19	28.7	5	26.6	4.9
LJL23	21	37.4	9.15	35.1	9.1
LJM10	19	18.8	8.73	16.7	8.6
LJL143	23	35	8.4	32.5	8.3
LJS142	20	18.9	6.43	16.7	6.5
LJL17	20	12.3	4.36	10.2	4.4
LJM06	19	18.6	8.79	16.5	8.7
LJM17	18	47.3	5.92	45.2	5.7
LJL04	17	31.1	10.1	29.3	10
LJM114	24	17	7.58	14.3	5.6
LJM111	18	45.2	4.9	43	4.9
LJM78	20	39.4	7.54	37.3	7.7
LJS238	20	6.9	7.92	4.8	6.7
LJS169	22	14.1	4.64	11.6	4.5
LJL11	24	63.4	6.49	60.8	6.7
LJL08	23	9.5	8.76	7	8.8
LJS105	19	9.5	4.85	7.4	4.7
LJL09	18	73	5.65	71.1	5.6
LJL38	20	4.8	3.66	2.5	3.3
LJM04	20	16.2	8.91	13.9	9
LJM26	17	50.7	5.77	48.8	5.8
LJS03	19	17.3	4.27	15.2	4.2
LJS192	23	12.1	4.29	9.7	4.2
LJM19	22	13.4	4.26	10.8	4.2
LJL138	19	45.9	9.42	43.8	9.5
LJL15	19	18.7	6.2	16.5	6.1
LJL91	19	18.5	5.82	16.4	5.8
LJM11	24	45.3	9.35	42.7	9.4
LJS138	20	18.5	5.88	16.2	5.5

Example 3

Antibodies against *Lu. longipalpis* saliva

It has previously been shown that sera from children living in an area endemic for VL have anti-SGS IgG antibodies that differentially recognize salivary gland antigens. Individuals with a positive anti-*Leishmania* DTH response exhibited anti-*Lu. longipalpis* saliva antibodies. A positive correlation was observed between anti-*Lu. longipalpis* saliva antibodies and anti-*Leishmania* DTH, but no correlation was observed between anti-saliva antibodies and anti-*Leishmania* serology (Barral *et al.*, *ibid*).

The change in humoral and cell-mediated anti-*Leishmania* responses in a 6-month follow up of individuals in an area endemic for VL as well as the change in anti-*Lu. longipalpis* saliva antibody responses in the same individuals was studied. Individuals ($n = 15$) who converted to positive anti-*Leishmania* DTH significantly increased their anti-*Lu. longipalpis* IgG (FIG. 1*A*; $P = 0.02$) and IgE antibody levels (FIG. 1B, $P = 0.002$). IgG1 was the principal antibody subclass involved in the increase of anti-saliva antibodies in the group converting anti-*Leishmania* DTH ($n = 15$) (FIG. 1C); no significant changes were observed in other IgG subclasses. The cut-off value for anti-*Lu. longipalpis* IgG in ELISAs was 0.045. A significant decrease in anti-saliva IgG antibody levels ($P = 0.035$) was observed in sera from children who converted their anti-*Leishmania* serology (Group I) (FIG. 1*A*). No significant changes were observed in anti-saliva IgE in Group I (FIG. 1*B*). Although IgG anti-saliva levels in Group II children decreased in the 6-month period, a significant increase in IgG4 anti-saliva was observed in this group ($P = 0.0245$; FIG. 1D).

The number and pattern of Lu. longipalpis salivary proteins recognized by the sera of individuals who converted either from $S^- \rightarrow S^+$ or from $DTH^- \rightarrow DTH^+$ was evaluated by Western blot. From seven randomly selected sera of individuals who converted their anti-Leishmania serology, two poorly recognized two different salivary proteins of 33 kDa and 200 kDa, respectively (FIG. 2A, lane 4); the remaining sera did not recognize any salivary protein at any time point. Conversely, from 13 randomly selected sera of $DTH^- \rightarrow DTH^+$ individuals, 12 recognized a variety of salivary proteins with various intensities. FIGS. 2A and 2B show the diversity of salivary antigens recognized by these sera (lanes 7-14). Additionally, sera from six $DTH^- \rightarrow DTH^+$ individuals showed an increase in the number and/or intensity of salivary proteins recognition when comparing time 0 (-) and 6 months (+) time points (FIG. 2A, lanes 7(-) and 8(+), 11(-) and 12(+), 13(-) and 14(+); FIG. 2B, lanes 11(-) and 12(+), 13(-) and 14(+), and data not shown). Some individuals in the $DTH^- \rightarrow DTH^+$ group did not show any change from time 0 to 6 months (FIG. 2A, lanes 9(-) and 10(+); FIG. 2B, lanes 7(-) and 8(+)) or did not recognize any salivary protein (FIG. 2B, lanes 9(-) and 10(+)).

The sera of the $DTH^- \rightarrow DTH^+$ individuals recognized a total of 16 different salivary proteins; however, the frequency of recognition varies among these individuals (FIG. 2C). A salivary protein of 45 kDa was recognized by 12 sera, followed by proteins of 44 and 43 and 35 kDa recognized by 8 sera (each), a protein of 17 kDa by 6 sera, and a protein of 16 kDa by 5 sera. Other salivary proteins were recognized as well but with less frequency (3 sera or less, FIG. 2C).

Thus, Group II children, who convert their anti-*Leishmania* DTH, also present an increase in anti-sand fly saliva antibodies as evidenced by ELISA and Western blot. A correlation between anti-saliva antibody titers and anti-*Leishmania* DTH has been shown (Barral *et al.*, *ibid*); the results presented herein show that development of anti-parasite DTH temporally coincides with development of anti-*Lu. longipalpis* saliva antibodies. Without being bound by theory, neutralization of sand fly salivary component(s) by antibodies or cellular response to salivary proteins allows for a more efficient mounting of an anti-*Leishmania* cell-mediated immune response, probably by developing a

Th1 response against the parasite. Sand fly saliva components, such as maxadilan, are able to impair macrophage function (Charlab *et al.*, *Proc Natl Acad Sci USA* 96:15155–60, 1999), which interferes with *Leishmania* survival and antigen presentation (Soares *et al.*, *J. Immunol.* 160:1811–6, 1998). The higher antibody levels observed in $DTH^- \rightarrow DTH^+$ individuals suggest that mounting an immune response against anti-saliva components is linked to developing cell-mediated immunity against *Leishmania*.

The results presently reported by Western blot analysis showed that individuals who converted their anti-*Leishmania* serology practically did not recognize any salivary protein whereas individuals who converted their anti-*Leishmania* DTH recognized a number of different salivary proteins. Frequency of salivary antigens recognized by these sera reveals a cluster of only a few proteins, including antigens with an approximate molecular mass of 45, 44, 43, 35, 27 and 16 kDa (FIG. 2C).

Among these antigens, the recognition of at least two salivary proteins (45 kDa and 35 kDa), represent two of the highest frequencies of recognition by human sera. Surprisingly, only two sera recognized a protein in the range of 6 kDa, the molecular weight of maxadilan (Titus and Ribeiro, *Parasitol Today* 6:157–159, 1990) suggesting that, in humans, maxadilan may not induce a strong antibody response, although it could be a strong inducer of cellular immunity.

Individuals who converted their anti-*Leishmania* cell-mediated immunity exhibited increased IgG1 and IgE levels. IgG1 has been related to a human Th1 response. Elevation of IgE antibodies suggests the development of an immediate hypersensitivity, since IgE is considered a marker of Th2-type responses. Without being bound by theory, it is likely that a mixed Th2-type (related to immediate hypersensitivity) and Th1-like response (related to DTH) against saliva components coexist in individuals who recently converted their anti-*Leishmania* DTH. In fact, this type of mixed response was reported in individuals exposed to insect bites, where the host immune response against insect saliva starts with DTH response and evolves to a predominant immediate-type hypersensitivity and finally desensitization (Melanby, *Nature*. 158, 554-555.13, 1946).

As disclosed herein, in mice, immunization using *Lu. longipalpis* salivary genes resulted in a typical DTH and/or antibody response to *Lu. longipalpis* salivary proteins (see below), suggesting that *Lu. longipalpis* bites could induce Th1 and Th2 responses in humans. Of interest, the *P. papatasii* (SP15) salivary protein responsible for the DTH response in mice is highly homologous to the SL1 protein present in *Lu. longipalpis* saliva (Charlab *et al.*, *Proc Natl Acad Sci USA* 96:15155–60, 1999). Without being bound by theory, the results presented herein suggest that a mixed anti-saliva response with both Th1 and Th2 components can help in establishing an anti-immune *Leishmania* response.

Example 4

DNA Vaccination in Mice

For genetic immunization, Swiss Webster mice were purchased from Taconic Farms. Mice were maintained in the NIAID Animal Care Facility under pathogen-free conditions. Mice were

inoculated in the right ear with 30 μg of the plasmid encoding the selected cDNA from *Lu. longipalpis* suspended in 5 μl of PBS. Each group is boosted 2 weeks later using the same regimen. Mice were challenged on the opposite ear with salivary gland homogenate of *Lu. longipalpis* and delayed type hypersensitivity (DTH) response is measured 24 hours after the injection by measuring thickness and redness of ear (++: at least 2 mice with a good DTH response, +++ : at least three mice had a good DTH response).

Table 2

DTH Response in Mice

***Lutzomyia longipalpis* salivary gland cDNA**	**DTH response (thickness and redness)**
pLJS201	-
pLJM19	++
pLJL91	-
pLJM06	-
pLJL15	+++
pLJM11	-
pLJM17	+++
pLJL11	-
pLJL08	++
pLJL18	++
pLJS142	-
pLJL13	-
pLJL34	++
pLJM111	+++
pLJL17	+++
pLJM04	-
pLJL23	++

*Delayed type hypersensitivity (DTH) response induced by injection of salivary gland homogenate on the ear of mice (group of three) previously immunized with salivary DNA vaccine. Mice were previously sensitized with specific DNA plasmids two times at two weeks interval then injected with salivary gland homogenate of the sand fly *Lutzomyia longipalpis*. DTH response was measured at 24 hours (tickness and redness of ear) after salivary gland homogenate injection. (++= at least 2 mice had good DTH response, +++ at least three mice had a good DTH response).

Example 5

Production of an Immune Response in Dogs

In a first experiment DTH (delayed type hypersensitivity) reaction is performed in dogs with natural immunity against the leishmaniasis in order to determine which *Lu. longipalpis* salivary proteins are recognized by a protective immune response. These dogs with natural immunity survived without symptoms after two years of exposure in an endemic area. In a second experiment naive dogs are immunized with the *Lu. longipalpis* salivary gland protein expressed by a plasmid in order to evaluate the capability to induce a cellular immune response measured by DTH.

Twelve dogs approximately three years old with natural immunity against Leishmaniasis are injected via an intradermal route (ID) in the back after shaving, with 100 µg of each individual plasmid suspended in 100 µl of PBS. Each plasmid is injected at a different point. The points are separated by at least 3 cm to avoid interference between DTH responses. The negative control (100 µl of buffer) is also inoculated by ID route.

The DTH response is assessed 72 hours after injection by measuring the larger diameter of the skin tumefaction area. The results are expressed as the mean value of the tumefaction area for all the dogs and as a percentage of dogs having a positive DTH response. A positive DTH is a tumefaction area diameter greater than or equal to 4 mm at 72 hours after injection.

In a second study, 10 naïve dogs 4 to 6 months old are immunized by ID injection in 10 points (100 µl per point) in the right ear with a pool of the plasmids encoding a *Lu. longipalpis* polypeptide, 100 µg for each one suspended in 1000 µl of PBS. On day 21, dogs are injected in 10 points (100 µl per point) in the left ear and in 10 points (100 µl per point) in the belly with a pool of the plasmids, 100 µg for each one suspended in 2000 µl of PBS. All dogs are challenged on day 35 by inoculation by ID route in the back (after shaving), with 100 µg of each individual plasmid suspended in 100 µl of PBS. Each plasmid is injected at a different point. The points are separated by at least 3 cm to avoid interference. As a negative control, 100 µl of buffer is inoculated intradermally. The DTH response is assessed 72 hours after challenge, by measuring the larger diameter of the skin tumefaction area. The results are expressed as the mean value of the tumefaction area for all the dogs and as a percentage of dogs having a positive DTH response. A positive DTH is a tumefaction area diameter higher or equal of 4 mm at 72 hours after injection.

The results of this study show that plasmids can induce a cellular immunity in dogs after injection, a cellular immunity reveled by a DTH response. The variation of the DTH response level can be by the variation of the expression of the insert.

It will be apparent that the precise details of the methods described may be varied or modified without departing from the spirit of the described disclosure. We claim all such modifications and variations that fall within the scope and spirit of the claims below.

CLAIMS

We claim:

1. A substantially purified salivary *Lu. longipalpis* polypeptide.

2. The polypeptide of claim 1, wherein the polypeptide comprises

a) an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67;

b) a conservative variant of the amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67;

c) an immunogenic fragment comprising at least eight consecutive amino acids of the amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, that specifically binds to an antibody that specifically binds the amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, respectively; or

d) the amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, and wherein administration of the polypeptide to a subject produces an immune response to *Lu. longipalpis*.

3. The *Lu. longipalpis* polypeptide of claim 2, wherein the polypeptide comprises an amino acid sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, or a conservative variant thereof.

4. The *Lu. longipalpis* polypeptide of claim 3, wherein the polypeptide comprises an amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67.

5. An antigenic fragment of the polypeptide of claim 4.

6. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence at least 80% identical to the amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67.

7. An isolated nucleic acid encoding the polypeptide of claim 1.

8. The nucleic acid of claim 7, wherein the nucleic acid comprises a sequence as set forth as SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 42, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 48, SEQ ID NO: 50, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 62, SEQ ID NO: 64, SEQ ID NO: 66, or SEQ ID NO: 68, or a degenerate variant thereof.

9. The nucleic acid of claim 7, wherein the nucleic acid comprises a sequence as set forth as SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 14, SEQ ID NO: 16,

SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 42, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 48, SEQ ID NO: 50, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 62, SEQ ID NO: 64, SEQ ID NO: 66, or SEQ ID NO: 68.

10. The nucleic acid of claim 7, wherein the nucleic acid encodes an amino acid sequence at least 80% identical to the amino acid sequence set forth as SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 42, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 48, SEQ ID NO: 50, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 62, SEQ ID NO: 64, SEQ ID NO: 66, or SEQ ID NO: 68.

11. The nucleic acid of claim 7, operably linked to an expression control sequence.

12. The nucleic acid of claim 11, wherein the expression control sequence is a promoter.

13. The nucleic acid of claim 12, wherein the promoter is an inducible or constitutive promoter.

14. The nucleic acid of claim 13, wherein the promoter is a cytomegalovirus promoter.

15. A vector comprising the nucleic acid of claim 7.

16. The vector of claim 15, wherein the vector is a plasmid.

17. The vector of claim 15, wherein the vector is a viral vector.

18. A host cell transformed with the vector of claim 15.

19. An antibody that specifically binds the polypeptide of claim 1.

20. The antibody of claim 19, wherein the antibody is a monoclonal antibody.

21. The antibody of claim 20, comprising a detectable label.

22. The antibody of claim 21, wherein the label is a fluorescent, enzymatic or radioactive label.

23. A pharmaceutical composition comprising the polypeptide of claim 1 and a pharmaceutically acceptable carrier.

24. A pharmaceutical composition comprising the nucleic acid of claim 7 and a pharmaceutically acceptable carrier.

25. A method for inducing an immune response to a *Lu. longipalpis* polypeptide in a subject, comprising:

administering to the subject a therapeutically effective amount of :

a) an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67;

b) a conservative variant of the amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67;

c) an immunogenic fragment comprising at least eight consecutive amino acids of the amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, that specifically binds to an antibody that specifically binds the amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, respectively; or

d) the amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49,

SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67; or

(e) a polynucleotide encoding the polypeptide set forth in (a), (b), (c), or (d),

thereby inducing the immune response to the *Lu. longipalpis* polypeptide in a subject.

26. The method of claim 25, wherein the immune response is a T cell response.

27. The method of claim 25, wherein the immune response is a B cell response.

28. The method of claim 25, wherein the subject is a non-human veterinary subject.

29. The method of claim 25, wherein the subject is a dog.

30. The method of claim 25, wherein the subject is a human.

31. A method for inhibiting a symptom of a *Leishmania* infection or preventing a *Leishmania* infection in a subject, comprising administering to the subject a therapeutically effective amount of:

a) an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67;

b) a conservative variant of the amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67;

c) an immunogenic fragment comprising at least eight consecutive amino acids of the amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, that specifically binds to an antibody that specifically binds the amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID

NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, respectively; or

d) the amino acid sequence set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67; or

(e) a polynucleotide encoding the polypeptide set forth in (a), (b), (c), or (d);

thereby inhibiting the symptom of the *Leishmania* infection or preventing the *Leishmania* infection.

32. Use of a composition comprising the polypeptide of claim 1 or a nucleic acid encoding the polypeptide of claim 1 for the manufacture of a medicament.

33. Use of the composition of claim 32, in conjunction with a composition comprising a *P. ariasi* or *a P. perniciosus* polypeptide for the manufacture of a medicament.

34. A method of diagnosing *Leishmania* infection in a subject, comprising:

contacting a solid substrate comprising at least three, six, or ten polypeptides, wherein each of the polypeptides comprises one amino acid sequence as set forth as SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, or SEQ ID NO: 67, or an immunogenic fragment thereof;

contacting the solid substrate with a sample obtained from the subject; and

detecting binding of a component of the sample to at least one polypeptide on the solid substrate, wherein detection of binding of the component to the substrate indicates that the subject is infected with *Leishmania*,

thereby diagnosing *Leishmania* infection in the subject.

35. The method of claim 34, wherein one of the at least three polypeptides comprises an amino acid sequence as set forth as SEQ ID NO: 1, wherein another of the at least three polypeptides

comprises an amino acid sequence as set forth as SEQ ID NO: 23, and wherein a further of the at least three polypeptides comprises an amino acid sequence as set forth as SEQ ID NO: 39.

36. The method of claim 34, wherein the solid substrate comprises at least six polypeptides, wherein a first polypeptide comprises an amino acid sequence as set forth as SEQ ID NO: 3, wherein a second polypeptide comprises an amino acid sequence as set forth as SEQ ID NO: 11, wherein a third polypeptide comprises an amino acid sequence as set forth as SEQ ID NO: 19, wherein a fourth polypeptide comprises an amino acid sequence as set forth as SEQ ID NO: 29, wherein a fifth polypeptide comprises an amino acid sequence as set forth as SEQ ID NO: 55, and wherein a sixth polypeptide comprises an amino acid sequence as set forth as SEQ ID NO: 59.

37. The method of claim 34, wherein the solid substrate comprises a polystyrene bead, a chip, a membrane, or a plate.

38. The method of claim 34, wherein detecting comprises contacting the component bound to the solid substrate with a labeled secondary antibody.

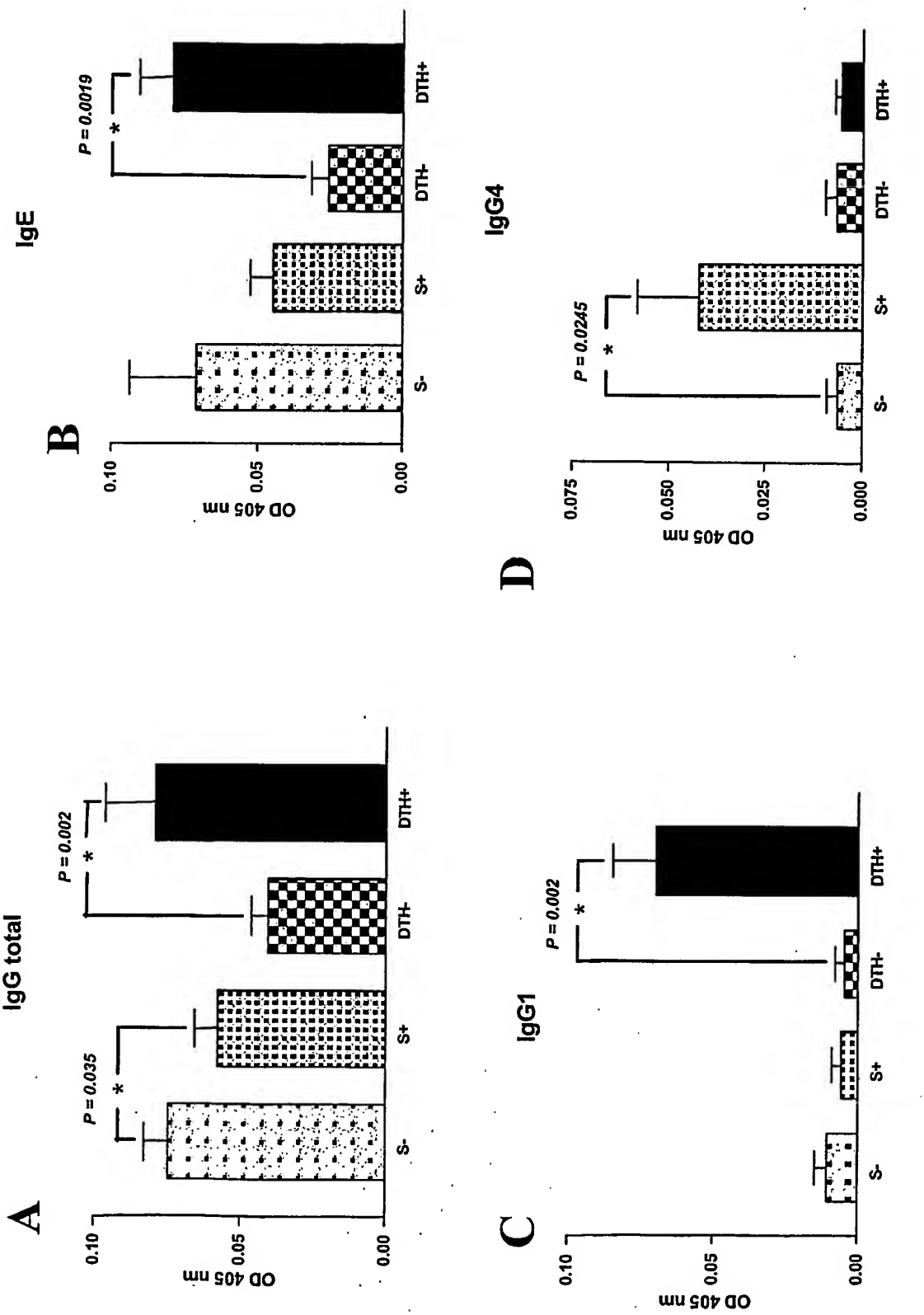

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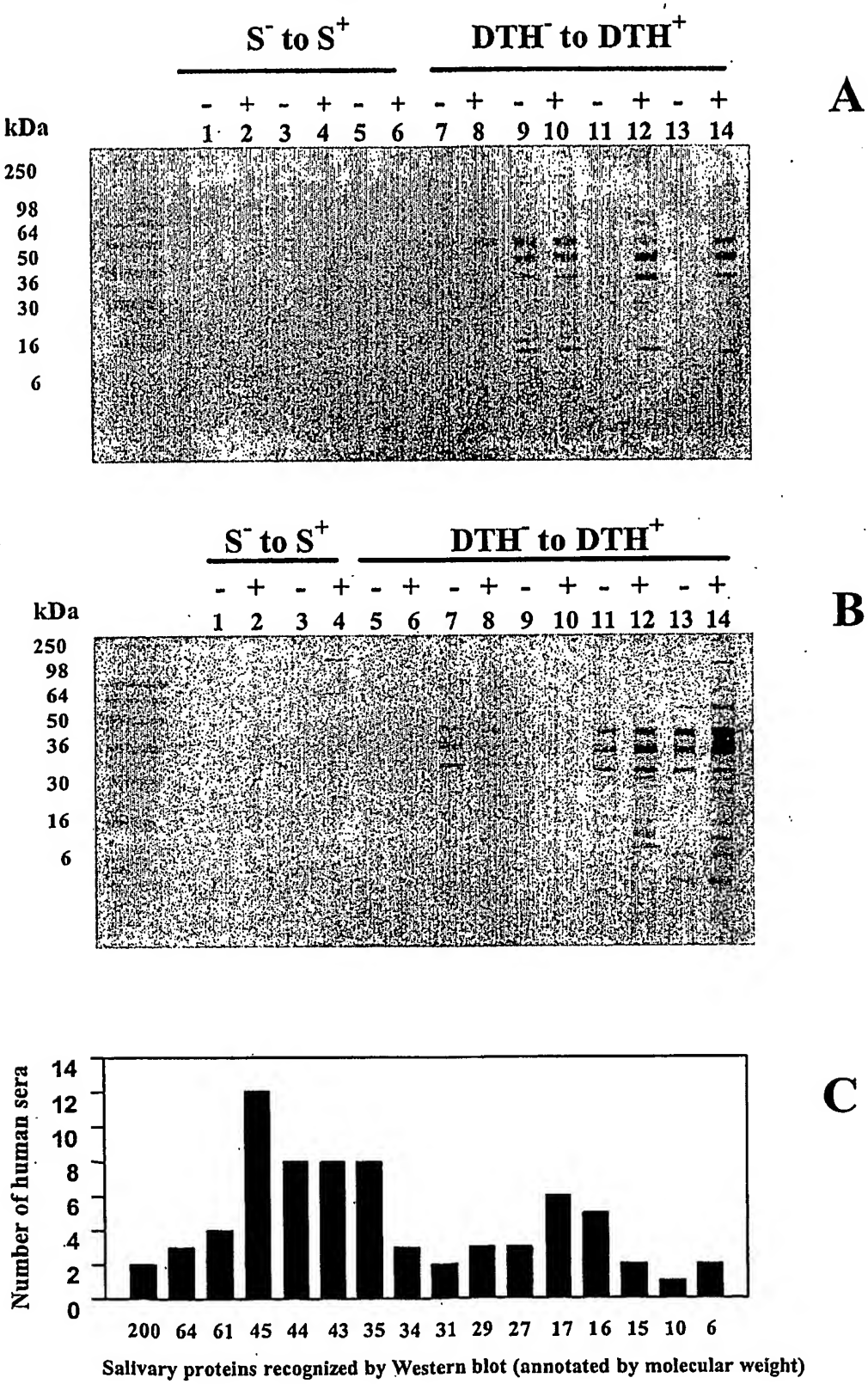
FIG. 1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Number of human sera
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2
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Salivary proteins recognized by Western blot (annotated by molecular weight)

FIG. 2

STATEMENT ACCOMPANYING SEQUENCE LISTING

The sequence listing does not include matter that goes beyond the disclosure in the international application.

The printout of the attached Sequence Listing is identical to the computer readable sequence listing on the enclosed computer disk.

SEQUENCE LISTING

<110> THE GOVERNMENT OF THE UNITED STATES OF AMERICA AS REPRESENTED BY THE SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES
Valenzuela, Jesus G.
Ribeiro, Jose M.C.
Barral, Aldina
Netto, Manoel
Brodskyn, Claudia
Gomes, Regis

<120> LUTZOMYIA LONGIPALPIS POLYPEPTIDES AND METHODS OF USE

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Cys Val Lys Asn Gly Tyr Thr Met Val Ser Ile Lys Thr Phe Glu Glu
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Asn Lys Glu Leu Leu Lys Glu Leu Lys Arg Val Ile Arg Thr Glu Asp
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Thr Gln Val Trp Ile Gly Gly Leu Lys His His Gln Phe Ala Asn Phe
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Arg Trp Val Ser Asp Gly Ser His Val Ala Thr Ala Ser Gly Tyr Thr
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Asn Trp Ala Pro Gly Glu Pro Ala Asp Ser Phe Tyr Tyr Asp Gln Phe
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35 40 45

Pro Phe Ser Leu Gly Ser Ile Lys Lys Leu Ile Glu Gln Gln Ile Pro
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Gly Ile His Val Val Ser Leu Lys Ile Gly Lys Ser Leu Ile Glu Asp
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Tyr Glu Ser Gly Phe Phe Val His Pro Asp Lys Gln Ile Gln Glu Val
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Cys Glu Ser Leu Gln Asn Asp Leu Thr Leu Ala Asn Gly Phe Asn Ala
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Ile Gly Phe Ser Gln Gly Ser Gln Phe Leu Arg Gly Leu Val Gln Arg
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Cys Glu Tyr Phe Arg Lys Leu Leu Asn Tyr Ala Ala Tyr Glu Lys Trp
165 170 175

Val Gln Lys Leu Leu Val Gln Ala Thr Tyr Trp His Asp Pro Leu Asn
180 185 190

Glu Asp Ala Tyr Arg Thr Gly Ser Thr Phe Leu Ala Asp Ile Asn Asn
195 200 205

Glu Arg Gln Ile Asn Asn Asp Tyr Ile Asn Asn Ile Arg Lys Leu Asn
210 215 220

Arg Phe Val Met Val Lys Phe Leu Asn Asp Ser Met Val Gln Pro Ile
225 230 235 240

Glu Ser Ser Phe Phe Gly Phe Tyr Ala Pro Gly Thr Asp Thr Glu Val
245 250 255

Leu Pro Leu Lys Gln Ser Lys Ile Tyr Leu Glu Asp Arg Leu Gly Leu
260 265 270

Gln Ser Val Pro Ile Asp Tyr Leu Glu Cys Gly Gly Asp His Leu Gln
275 280 285

Phe Thr Lys Glu Trp Phe Ile Lys Phe Ile Ile Pro Tyr Leu Lys Gln
290 295 300

<210> 6
<211> 1273
<212> DNA
<213> Lutzomyia longipalpis

<400> 6
tacttcgtac tctcagaatt tcttacaagt tccttttttct cttaactttt aaagttttat 60

ttaacaaaat tgctccattt tttcgttttc tgaatattct gttgaaattt tgattaatct 120

attttatgtg cagtttttac taaaaatccc ttatcagcaa cccggtgtct acagttttgt 180

cacgctcagt agcatcttca aggtggtaag aaaaaatgaa actcctgcaa atcatcttct 240

ctctcttcct ggtctttttc ccgacctcaa atggggccct gaccggaaat gaaagtgcag 300

caaatgcagc tcccttgcct gtcgtcctgt ggcacgggat gggcgattct tgctgctttc 360

ccttcagttt gggaagcata aaaaaattaa ttgaacaaca aattcctggg attcatgttg 420

ttagcctgaa aattggaaag tctctcattg aggactatga aagtggattt tttgttcatc 480

cagacaagca aattcaggaa gtttgtgagt cacttcagaa cgatctaaca ctcgcaaatg 540

gattcaatgc aattggattt tctcagggta gtcagttcct gcgaggtctt gtgcaacgat 600

gttcttctat acaagtaagg aatctcattt ccattggagg acagcatcaa ggggtttttg 660

gtctgcccta ttgtccttcg ttgagcagaa agacttgcga atactttaga aagctcctga 720

attatgcagc ttatgaaaaa tgggtacaga aactcctagt tcaagccacc tactggcatg 780

atcctctaaa tgaggatgca tatcggactg gaagcacttt ccttgctgat ataaataatg 840

agagacaaat caataatgac tatattaata atattcggaa gctaaatcgt tttgtgatgg 900

taaagttcct caacgacagc atggttcagc caattgaatc tagtttcttt ggattctacg 960

ctccaggaac tgatacagaa gttctcccat taaaacaaag caagatttat ttggaagatc 1020

gtttgggact tcaatcagta ccgatagatt atctagaatg cggaggagat catttgcaat 1080

ttacaaaaga atggttcata aagtttatca taccctatct gaagcaataa gagctgcaat 1140

gtaattgatt aaaaaatgtt aaccatttca ggatgattgg gtgacccctt aaaaatataa 1200

atgaaaaaat atacaaaaga aataaatttt tatattgatc ccacaaaaaa aaaaaaaaaa 1260

aaaaaaaaaa aaa 1273

<210> 7
<211> 102
<212> PRT
<213> Lutzomyia longipalpis

<400> 7

Met Arg Asn Phe Ala Val Val Ser Leu Ala Val Ala Val Leu Leu Phe
1 5 10 15

Cys Ala Trp Pro Ile Asn Ala Glu Asp Asn Glu Glu Val Gly Lys Ala
20 25 30

Arg Glu Lys Arg Gly Leu Lys Asp Ala Met Glu His Phe Lys Asn Gly
35 40 45

Phe Lys Glu Leu Thr Lys Asp Phe Lys Leu Pro Ser Leu Pro Ser Leu
50 55 60

Pro Gly Phe Gly Lys Lys Pro Glu Ser Gly Ser Ser Glu Asp Ser Gly
65 70 75 80

Asp Lys Thr Glu Asp Thr Ser Gly Ser Lys Asp Asp Gln Ser Lys Asp
85 90 95

Asn Thr Val Glu Glu Ser
100

<210> 8
<211> 466
<212> DNA
<213> Lutzomyia longipalpis

<400> 8
ggatcggcca ttatggccgg ggcagttaat cgccacaatt taataaaatg aggaactttg 60

ctgtagtcag tttagccgtt gctgtcctgc tcttctgtgc atggcctata aatgcggaag 120

ataatgaaga agttggaaag gcgagagaaa aaagaggctt aaaagacgca atggaacact 180

tcaaaaatgg atttaaggag ctgacaaagg actttaaact tccaagcctt ccaagtcttc 240

ctggatttgg taaaaagcct gaatctggaa gttctgaaga ttctggagat aaaactgagg 300

ataccagtgg atctaaggac gaccaatcaa aggataatac ggtcgaagaa tcttaagaaa 360

ggcgcaaata gctattttca aagtggcgaa tgtttctttc tttatctgaa ataaatattt 420

ttaaaccttt cgaaaccaaa aaaaaaaaaa aaaaaaaaaa aaaaaa 466

<210> 9
<211> 247
<212> PRT
<213> Lutzomyia longipalpis

<400> 9

Met Asn Phe Leu Leu Lys Ile Phe Ser Leu Leu Cys Leu Cys Gly Leu
1 5 10 15

Gly Tyr Ser Trp Gln Asp Val Arg Asn Ala Asp Gln Thr Leu Trp Ala
20 25 30

Tyr Arg Ser Cys Gln Lys Asn Pro Glu Asp Lys Asp His Val Pro Gln
35 40 45

Trp Arg Lys Phe Glu Leu Pro Asp Asp Glu Lys Thr His Cys Tyr Val
50 55 60

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Lys Cys Val Trp Thr Arg Leu Gly Ala Tyr Asn Glu Asn Glu Asn Val
65                  70                  75                  80

Phe Lys Ile Asp Val Ile Thr Lys Gln Phe Asn Glu Arg Gly Leu Glu
                85                  90                  95

Val Pro Ala Gly Leu Asp Gln Glu Leu Gly Gly Ser Thr Asp Gly Thr
            100                 105                 110

Cys Lys Ala Val Tyr Asp Lys Ser Met Lys Phe Phe Lys Ser His Phe
        115                 120                 125

Met Asp Phe Arg Asn Ala Tyr Tyr Ala Thr Tyr Asp Gly Ser Asp Glu
    130                 135                 140

Trp Phe Ser Lys Asn Pro Asp Val Lys Pro Lys Gly Thr Lys Val Ser
145                 150                 155                 160

Glu Tyr Cys Lys Asn Lys Asp Asp Gly Asp Cys Lys His Ser Cys Ser
                165                 170                 175

Met Tyr Tyr Tyr Arg Leu Ile Asp Glu Asp Asn Leu Val Ile Pro Phe
            180                 185                 190

Ser Asn Leu Pro Asp Tyr Pro Glu Asp Lys Leu Glu Glu Cys Arg Asn
        195                 200                 205

Glu Ala Lys Ser Ala Asn Glu Cys Lys Ser Ser Val Ile Tyr Gln Cys
    210                 215                 220

Leu Glu Asn Ala Asp Lys Ser Ala Leu Asp Ala Ser Leu Asn Ile Leu
225                 230                 235                 240

Asp Glu Phe Ser Gly Arg Tyr
                245
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<210> 10
<211> 955
<212> DNA
<213> Lutzomyia longipalpis

<400> 10

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tctctgtgga ctggggtatt catggcagga tgtgagaaat gccgatcaaa ccctctgggc    120

gtatagatcg tgccaaaaga atcctgaaga taaggatcac gtacctcaat ggaggaagtt    180

cgaattaccc gacgatgaaa agactcattg ctacgtcaag tgcgtatgga cgcgtttggg    240
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agcttacaat gaaaatgaaa atgttttcaa aattgatgtc attactaagc aatttaatga 300

acgtggccta gaagttccgg ctggacttga tcaagaattg ggtggttcta cagatggaac 360

ttgcaaagca gtttacgata aatccatgaa gttcttcaaa tctcatttta tggactttag 420

gaatgcttac tacgcaactt atgacggttc tgatgaatgg tttagcaaga accctgatgt 480

aaaaccgaaa ggaacaaaag tttccgaata ctgcaaaaat aaagatgatg gagattgcaa 540

acattcctgc agtatgtact actaccgctt aatcgatgaa gacaacttag ttattccgtt 600

cagcaactta cctgactatc ccgaagataa gctcgaggaa tgcaggaatg aagccaagtc 660

cgcaaatgag tgcaaatcat ctgttatcta tcagtgtttg gaaaatgcgg ataagtcagc 720

tttagacgcg tctttgaata tactcgatga gttttctgga agatattaaa acaaactgga 780

taaaaaactt aggccaacct atgattcgaa cttacgattt tgaacttgaa attcatgtgc 840

tttaacctat tgtcccacta ggaagaaaaa tccatatttg gtgatgttaa actatttttg 900

aacctcttca aaataaacaa ttttcaaaaa aaaaaaaaaa aaaaaaaaaa aaaaa 955

<210> 11
<211> 325
<212> PRT
<213> Lutzomyia longipalpis

<400> 11

Met Phe Leu Lys Trp Val Val Cys Ala Phe Ala Thr Val Phe Leu Val
1 5 10 15

Gly Val Ser Gln Ala Ala Pro Pro Gly Val Glu Trp Tyr His Phe Gly
20 25 30

Leu Ile Ala Asp Met Asp Lys Lys Ser Ile Ala Ser Asp Lys Thr Thr
35 40 45

Phe Asn Ser Val Leu Lys Ile Asp Glu Leu Arg His Asn Thr Lys Thr
50 55 60

Asp Gln Tyr Ile Tyr Val Arg Ser Arg Val Lys Lys Pro Val Ser Thr
65 70 75 80

Arg Tyr Gly Phe Lys Gly Arg Gly Ala Glu Leu Ser Glu Ile Val Val
85 90 95

Phe Asn Asn Lys Leu Tyr Thr Val Asp Asp Lys Ser Gly Ile Thr Phe
100 105 110

Arg Ile Thr Lys Asp Gly Lys Leu Phe Pro Trp Val Ile Leu Ala Asp
115 120 125

Ala Asp Gly Gln Arg Pro Asp Gly Phe Lys Gly Glu Trp Ala Thr Ile
130 135 140

Lys Asp Asp Thr Ile Tyr Val Gly Ser Thr Gly Met Leu Lys Phe Thr
145 150 155 160

Ser Ser Leu Trp Val Lys Lys Ile Thr Lys Asp Gly Val Val Thr Ser
165 170 175

His Asp Trp Thr Asp Lys Tyr Arg Lys Ile Leu Lys Ala Leu Asn Met
180 185 190

Pro Asn Gly Phe Val Trp His Glu Ala Val Thr Trp Ser Pro Phe Arg
195 200 205

Lys Gln Trp Val Phe Met Pro Arg Lys Cys Ser Arg His Pro Phe Ser
210 215 220

Gln Glu Leu Glu Glu Arg Thr Gly Cys Asn Lys Ile Val Thr Ala Asp
225 230 235 240

Glu Asn Phe Asn Asp Ile Gln Val Ile His Ile Gln Asp Gln Pro Tyr
245 250 255

Asn Leu Ala Ser Gly Phe Ser Ser Phe Arg Phe Ile Pro Gly Thr Lys
260 265 270

Asn Glu Arg Leu Leu Ala Leu Arg Thr Val Glu Gln Glu Asp Gln Val
275 280 285

Lys Thr Trp Ala Val Val Met Asp Met Lys Gly Thr Val Leu Met Tyr
290 295 300

Glu Lys Glu Leu Tyr Asp Glu Lys Phe Glu Gly Leu Ala Phe Phe Gly
305 310 315 320

Gly Ile Lys Lys Asn
325

<210> 12
<211> 1071
<212> DNA
<213> Lutzomyia longipalpis

<400> 12
aaagagaagt agtgagaatg tttcttaagt gggttgtttg tgcttttgcg actgtcttcc 60

ttgttggggt gagtcaggca gccccaccgg gggttgaatg gtatcacttt ggtctgattg 120

ctgatatgga caaaaaatcc atcgcgagtg acaaaaccac ctttaacagc gtcctaaaga 180

tcgatgaatt gcgccacaac acaaaaacgg atcaatacat ttatgtgcgt agtcgagtga 240

agaagcccgt ttccacgagg tatgggttca aaggacgcgg tgcggaattg tcggaaattg 300

ttgtcttcaa caataaactt tacacagttg atgataaatc tggaattacg ttccgcataa 360

cgaaagacgg aaaactcttc ccgtgggtta ttctcgcaga tgccgatgga cagcgacccg 420

atggctttaa gggtgaatgg gctacaatta aggatgatac aatctatgtt ggatctacgg 480

ggatgctcaa gttcacttca tccctttggg tgaagaagat cacgaaagat ggcgttgtta 540

cgagtcacga ttggactgat aaataccgaa agattctcaa agctctaaac atgccaaatg 600

gttttgtctg gcatgaggct gttacgtggt ctccattcag gaagcaatgg gtcttcatgc 660

cgagaaagtg ctcaaggcat cccttctcac aggaactcga agaacgcaca gggtgcaata 720

aaatagtgac ggcagatgag aatttcaacg acattcaagt tattcacatt caagatcagc 780

catataattt agcttctggt ttctcttcct tccgctttat tcctggtacg aaaaatgaaa 840

gacttctcgc cttgaggaca gtagagcagg aagatcaggt taaaacttgg gctgtggtca 900

tggatatgaa aggaacagtt ctgatgtacg aaaaggaact ttatgacgaa aaattcgaag 960

gtttagcatt ctttggtggt attaaaaaga attaatttgt tccagaagct tttagatgaa 1020

ataataaatt ttatttcatt ttaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 1071

<210> 13
<211> 160
<212> PRT
<213> Lutzomyia longipalpis

<400> 13

Met Ala Leu Lys Phe Leu Pro Val Leu Leu Leu Ser Cys Phe Ala Met
1 5 10 15

Ser Thr Ala Leu Gln Val Thr Glu Lys Glu Leu Ser Asp Gly Lys Lys
20 25 30

Ile Phe Ile Ser Lys Val Glu Leu Asn Trp Phe Glu Ala Leu Asp Phe
35 40 45

Cys Ile His Arg Gly Leu Thr Leu Leu Ser Ile Lys Ser Ala Lys Glu
50 55 60

Asn Val Asp Val Thr Lys Ala Ile Arg Ala Glu Leu Asn Phe Asp Ser
65 70 75 80

Lys Lys Leu Ala His Val Trp Thr Gly Gly Ile Arg His Ser Gln Asp
85 90 95

Lys Tyr Phe Arg Trp Ile Asn Asp Gly Thr Lys Val Val Lys Arg Val
100 105 110

Tyr Thr Asn Trp Phe Thr Gly Glu Pro Asn Asn Gly Tyr Trp Lys Asp
115 120 125

Glu Phe Cys Leu Glu Ile Tyr Tyr Lys Thr Glu Glu Gly Lys Trp Asn
130 135 140

Asp Asp Lys Cys His Val Lys His His Phe Val Cys Gln Glu Lys Lys
145 150 155 160

<210> 14
<211> 648
<212> DNA
<213> Lutzomyia longipalpis

<400> 14
cgcggccgcg tcgaccgaca gaaggggtag tttgtagaga actttgagtt ctaaaggaaa 60

ttctcaagaa gaaaatattc aaaagtaaag aatggcgttg aagtttcttc cggttctcct 120

tctaagctgc ttcgcaatga gcacggcact acaagttact gagaaggaac tttctgatgg 180

gaaaaagatc ttcatctcca aagttgagct aaactggttc gaagctcttg atttctgtat 240

ccatcgtggt cttacgttgc tctcaattaa atccgccaag gaaaatgtag acgtaacaaa 300

agcaattcgg gctgaattga attttgattc aaagaaattg gctcatgtgt ggactggagg 360

tattcgccat agtcaagata agtatttccg ttggataaat gatggaacta aagttgttaa 420

acgagtctac accaattggt tcactggaga accaaataat ggttactgga aggatgaatt 480

ttgtctggaa atttactata aaaccgaaga agggaagtgg aatgatgata aatgtcacgt 540

gaagcatcat tttgtatgtc aagaaaagaa ataaattgat tgattttgtt tgctgatttg 600

cagttcagaa ttgaaaagcc aaaaaaaaaa aaaaaaaaaa aaaaaaaa 648

<210> 15
<211> 301
<212> PRT
<213> Lutzomyia longipalpis
<400> 15

Met Asn Ser Ile Asn Phe Leu Ser Ile Val Gly Leu Ile Ser Phe Gly
1 5 10 15

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Phe Ile Val Ala Val Lys Cys Asp Gly Asp Glu Tyr Phe Ile Gly Lys
            20                  25                  30

Tyr Lys Glu Lys Asp Glu Thr Leu Phe Phe Ala Ser Tyr Gly Leu Lys
        35                  40                  45

Arg Asp Pro Cys Gln Ile Val Leu Gly Tyr Lys Cys Ser Asn Asn Gln
    50                  55                  60

Thr His Phe Val Leu Asn Phe Lys Thr Asn Lys Lys Ser Cys Ile Ser
65                  70                  75                  80

Ala Ile Lys Leu Thr Ser Tyr Pro Lys Ile Asn Gln Asn Ser Asp Leu
                85                  90                  95

Thr Lys Asn Leu Tyr Cys Gln Thr Gly Gly Ile Gly Thr Asp Asn Cys
            100                 105                 110

Lys Leu Val Phe Lys Lys Arg Lys Arg Gln Ile Ala Ala Asn Ile Glu
        115                 120                 125

Ile Tyr Gly Ile Pro Ala Lys Lys Cys Ser Phe Lys Asp Arg Tyr Ile
    130                 135                 140

Gly Ala Asp Pro Leu His Val Asp Ser Tyr Gly Leu Pro Tyr Gln Phe
145                 150                 155                 160

Asp Gln Glu His Gly Trp Asn Val Glu Arg Tyr Asn Ile Phe Lys Asp
                165                 170                 175

Thr Arg Phe Ser Thr Glu Val Phe Tyr His Lys Asn Gly Leu Phe Asn
            180                 185                 190

Thr Gln Ile Thr Tyr Leu Ala Glu Glu Asp Ser Phe Ser Glu Ala Arg
        195                 200                 205

Glu Ile Thr Ala Lys Asp Ile Lys Lys Lys Phe Ser Ile Ile Leu Pro
    210                 215                 220

Asn Glu Glu Tyr Lys Arg Ile Ser Phe Leu Asp Val Tyr Trp Phe Gln
225                 230                 235                 240

Glu Thr Met Arg Lys Lys Pro Lys Tyr Pro Tyr Ile His Tyr Asn Gly
                245                 250                 255
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Glu Cys Ser Asn Glu Asn Lys Thr Cys Glu Leu Val Phe Asp Thr Asp
260 265 270

Glu Leu Met Thr Tyr Ala Leu Val Lys Val Phe Thr Asn Pro Glu Ser
275 280 285

Asp Gly Ser Arg Leu Lys Glu Glu Asp Leu Gly Arg Gly
290 295 300

<210> 16
<211> 1021
<212> DNA
<213> Lutzomyia longipalpis

<400> 16
cttctttgga tttattgagt gattaacagg aaattagctg aagaaatgaa ttcgattaat 60

ttcctatcaa tagttggttt aatcagtttt ggattcattg ttgcagtaaa gtgtgatggt 120

gatgaatatt tcattggaaa atacaaagaa aaagatgaga cactgttttt tgcaagctac 180

ggcctaaaga gggatccttg ccaaattgtc ttaggctaca aatgctcaaa caatcaaacc 240

cactttgtgc ttaattttaa aaccaataag aaatcctgca tatcagcaat taagctgact 300

tcttacccaa aaatcaatca aaactcggat ttaactaaaa atctctactg ccaaactgga 360

ggaataggaa cagataactg caaacttgtc ttcaagaaac gtaaaagaca aatagcagct 420

aatattgaaa tctacggcat tccagcgaag aaatgttcct tcaaggatcg ttacattgga 480

gctgatccac tccacgtcga ttcctatggg cttccgtatc agtttgatca ggaacatgga 540

tggaatgtgg aacgatataa cattttcaaa gacacaagat tttccacaga agttttctac 600

cacaaaaatg gtttatttaa cacccaaata acttatttgg ctgaagaaga ttccttctct 660

gaagctcgag agattactgc gaaggatatt aagaagaagt tttcaattat tttgcccaat 720

gaagagtata agaggattag tttcttggac gtttattggt tccaggagac tatgcgaaaa 780

aagcctaaat atccctacat tcactacaat ggagaatgca gcaatgagaa taaaacttgt 840

gaacttgtct ttgacaccga tgaactaatg acctacgccc ttgttaaagt ctttactaat 900

cctgagagtg atggatctag gctcaaagaa gaggatttgg gaagaggata aatcttctta 960

ataaaaaaaa gttctgtaag aaaatattgt tcaataaatt aaaaaaaaaa aaaaaaaaaa 1020

a 1021

<210> 17
<211> 161
<212> PRT
<213> Lutzomyia longipalpis

<400> 17

Met Ala Phe Ser Asn Thr Leu Phe Val Leu Phe Val Ser Phe Leu Thr
1 5 10 15

Phe Cys Gly Ala Asp Gln Thr Leu Ile Glu Lys Glu Leu Thr Gly Arg
20 25 30

Thr Val Tyr Ile Ser Lys Ile Lys Leu Asn Trp Asn Asp Ala Phe Asp
35 40 45

Tyr Cys Ile Arg Asn Gly Leu Thr Phe Ala Lys Ile Lys Ser Ala Glu
50 55 60

Glu Asn Thr Glu Leu Ser Glu Lys Leu Lys Thr Val Ile Arg Thr Glu
65 70 75 80

Glu Phe Gln Val Trp Ile Gly Gly Ile Glu His His Gln Asp Ser Ser
85 90 95

Phe Arg Trp Val Ser Asp Ser Gln Pro Ile Thr Asn Lys Leu Gly Tyr
100 105 110

115 120 125

Glu Tyr Cys Leu Glu Ile Leu Phe Arg Lys Glu Asp Gly Lys Trp Asn
130 135 140

Asp Phe Pro Cys Ser Ala Arg His His Phe Val Cys Glu Lys Arg Thr
145 150 155 160

Lys

<210> 18
<211> 586
<212> DNA
<213> Lutzomyia longipalpis

<400> 18
aatagatctt caaaacgtct aagaatggct ttcagcaaca ctttatttgt tctttttgtg 60
agtttttaa cgttttgtgg cgctgatcag acacttattg agaaggaatt aaccggaaga 120

actgtttata tctccaaaat taagctaaat tggaacgatg ccttcgatta ctgcatccgc 180

aatggcctca cctttgctaa gattaaatca gctgaagaaa acaccgaact gagtgagaaa 240

ctcaagacag tcattcgtac ggaggagttt caagtttgga ttggaggcat tgaacatcat 300

caagacagtt ccttccgctg ggtaagcgac tcccaaccaa taaccaacaa attgggctac 360

aaatacacaa actggaatac cggagagccc acaaattacc aaaacaacga atattgcttg 420

gaaatattat tccggaagga agatggaaaa tggaatgatt ttccctgcag tgcaagacat 480

cattttgttt gtgaaaaaag aacaaaataa aatgaagaaa atgtgatttt cctttggttg 540

aagaataaaa ttctgttgaa aaaaaaaaaa aaaaaaaaaa aaaaaa 586

<210> 19
<211> 105
<212> PRT
<213> Lutzomyia longipalpis

<400> 19

Met Gln Asn Phe Leu Leu Val Ser Leu Ala Leu Ala Ala Leu Met Leu
1 5 10 15

Cys Ala Glu Ala Lys Pro Tyr Asp Phe Pro Leu Tyr Gln Asp Leu Ile
20 25 30

Gln Gly Val Ile Gln Arg Glu Ser Gln Ala Glu Arg Glu Lys Arg Ser
35 40 45

Pro Asn Glu Asp Tyr Glu Lys Gln Phe Gly Asp Ile Val Asp Gln Ile
50 55 60

Lys Glu Ile Ser Phe Asn Val Met Lys Met Pro His Phe Gly Ser Ser
65 70 75 80

Asp Asp Asn Arg Asp Asp Gly Glu Tyr Val Asp His His Tyr Gly Asp
85 90 95

Glu Asp Asp Arg Asp Tyr Asp His Tyr
100 105

<210> 20
<211> 457
<212> DNA
<213> Lutzomyia longipalpis

<400> 20
atttagtttg tgtttaacaa aacaagaatg cagaacttcc ttttagtttc cttggcttta 60

gctgccttaa tgctatgtgc cgaagcaaag ccgtacgatt ttccgcttta tcaggactta 120

attcagggcg ttattcagcg cgaaagtcaa gctgagaggg agaagagaag ccccaatgag 180

gactatgaga agcaatttgg ggatattgtt gatcaaatta aggaaattag tttcaatgtc 240

atgaaaatgc cccattttgg aagctctgat gataatcgtg atgatggcga gtacgttgat 300

catcattatg gtgacgaaga tgatcgtgat tatgatcatt actaaatact acttgctcct 360

gctgaatgac ttgaaggaat catttttttg caaaaatatc catcaaatta ttgaattaat 420

aaagttgcaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 457

<210> 21
<211> 157
<212> PRT
<213> Lutzomyia longipalpis

<400> 21

Met Lys Phe Tyr Ile Phe Gly Val Phe Leu Val Ser Phe Leu Ala Leu
1 5 10 15

Cys Asn Ala Glu Asp Tyr Asp Lys Val Lys Leu Thr Gly Arg Thr Val
20 25 30

Tyr Ile Ser Arg Ser Lys Ala Pro Trp Phe Thr Ala Leu Asp Asn Cys
35 40 45

Asn Arg Arg Phe Thr Phe Ala Met Ile Lys Ser Gln Lys Glu Asn Glu
50 55 60

Glu Leu Thr Asn Ala Leu Leu Ser Val Ile Lys Ser Asp Glu Glu Asn
65 70 75 80

Val Trp Ile Gly Gly Leu Arg His Asp Leu Asp Asp Tyr Phe Arg Trp
85 90 95

Ile Ser Phe Gly Thr Ala Leu Ser Lys Thr Ser Tyr Thr Asn Trp Ala
100 105 110

Pro Lys Glu Pro Thr Gly Arg Pro His Arg Thr Gln Asn Asp Glu Phe
115 120 125

130 135 140

Cys Trp Arg Lys Arg Leu Tyr Val Cys Glu Lys Arg Asp
145 150 155

<210> 22
<211> 596
<212> DNA
<213> Lutzomyia longipalpis

<400> 22
gtttaaggaa tttctttcat ctcagtcttc gattttcttt aaacaaataa tgaagtttta 60

tatttttgga gttttcctgg tgagctttct tgcattatgc aatgctgagg attatgataa 120

agtaaaactt actggaagaa ctgtttacat ctccagatca aaggctccgt ggttcacagc 180

tttagacaat tgtaatcgtt tacgcttcac cttcgccatg atcaagtctc agaaggagaa 240

tgaagagcta acaaatgcgc ttttaagtgt aattaaatct gacgaagaaa atgtttggat 300

tggaggtctt aggcacgatc tggatgacta cttccgttgg attagttttg gaactgcatt 360

gtcaaagact tcgtacacca attgggcccc aaaggaaccc acaggaaggc cccatagaac 420

tcaaaatgat gaattctgca tgcaaatgtc tttcaaagat ggtggcaaat ggagtgataa 480

cacctgttgg cgtaaacgtt tgtacgtttg tgaaaagcgt gattaaataa aggaacactg 540

ccaatgaata ttgggcaatt tgagagaaat taaattaaaa aaaaaaaaaa aaaaaa 596

<210> 23
<211> 412
<212> PRT
<213> Lutzomyia longipalpis

<400> 23

Met Arg Phe Phe Phe Val Phe Leu Ala Ile Val Leu Phe Gln Gly Ile
1 5 10 15

His Gly Ala Tyr Val Glu Ile Gly Tyr Ser Leu Arg Asn Ile Thr Phe
20 25 30

Asp Gly Leu Asp Thr Asp Asp Tyr Asn Pro Lys Phe Asn Ile Pro Thr
35 40 45

Gly Leu Ala Val Asp Pro Glu Gly Tyr Arg Leu Phe Ile Ala Ile Pro
50 55 60

Arg Arg Lys Pro Lys Val Pro Tyr Thr Val Ala Glu Leu Asn Met Val
65 70 75 80

Met Asn Pro Gly Phe Pro Val Glu Arg Ala Pro Ser Phe Glu Lys Phe
85 90 95

Lys Lys Phe Asn Gly Glu Gly Lys Lys Asp Leu Val Asn Val Tyr Gln
100 105 110

Pro Val Ile Asp Asp Cys Arg Arg Leu Trp Val Leu Asp Ile Gly Lys
115 120 125

Val Glu Tyr Thr Gly Gly Asp Ala Asp Gln Tyr Pro Lys Gly Lys Pro
130 135 140

Thr Leu Ile Ala Tyr Asp Leu Lys Lys Asp His Thr Pro Glu Ile His
145 150 155 160

Arg Phe Glu Ile Pro Asp Asp Leu Tyr Ser Ser Gln Val Glu Phe Gly
165 170 175

Gly Phe Ala Val Asp Val Val Asn Thr Lys Gly Asp Cys Thr Glu Ser
180 185 190

Phe Val Tyr Leu Thr Asn Phe Lys Asp Asn Ser Leu Ile Val Tyr Asp
195 200 205

Glu Thr Gln Lys Lys Ala Trp Lys Phe Thr Asp Lys Thr Phe Glu Ala
210 215 220

225 230 235 240

Lys Val Gly Leu Phe Gly Ile Ala Leu Gly Asp Arg Asp Glu Met Gly
245 250 255

His Arg Pro Ala Cys Tyr Ile Ala Gly Ser Ser Thr Lys Val Tyr Ser
260 265 270

Val Asn Thr Lys Glu Leu Lys Thr Glu Asn Gly Gln Leu Asn Pro Gln
275 280 285

Leu His Gly Asp Arg Gly Lys Tyr Thr Asp Ala Ile Ala Leu Ala Tyr
290 295 300

Asp Pro Glu His Lys Val Leu Tyr Phe Ala Glu Ser Asp Ser Arg Gln
305 310 315 320

Val Ser Cys Trp Asn Val Asn Met Glu Leu Lys Pro Asp Asn Thr Asp
325 330 335

Val Ile Phe Ser Ser Ala Arg Phe Thr Phe Gly Thr Asp Ile Leu Val
340 345 350

Asp Ser Lys Gly Met Leu Trp Ile Met Ala Asn Gly His Pro Pro Val
355 360 365

Glu Asp Gln Glu Lys Ile Trp Lys Met Arg Phe Val Asn Arg Lys Ile
370 375 380

Arg Ile Met Lys Val Asp Thr Glu Arg Val Phe Lys Tyr Ser Arg Cys

385 390 395 400

Asn Pro Asn Tyr Lys Pro Pro Lys Glu Ile Glu Val
405 410

<210> 24
<211> 1409
<212> DNA
<213> Lutzomyia longipalpis

<400> 24
agtcagtgtt aatgaagaaa ttgcaattat gaggttcttc tttgttttcc ttgccatcgt 60

ccttttcaa gggatccacg gagcttatgt ggaaatagga tattctctga gaaatattac 120

attcgatgga ttggatacag atgactacaa tccaaagttc aacattccaa cgggtttggc 180

agttgatccc gaaggatata ggctcttcat agccatccca aggagaaagc caaaggttcc 240

ctacactgtg gctgaactga atatggtcat gaatcccgga tttcccgtcg agagagctcc 300

gagctttgag aaattcaaaa aattcaatgg cgagggcaaa aaggatcttg ttaatgtgta 360

tcagccagtc attgatgatt gtcgtcgtct ttgggtgctt gacattggga aggtggaata 420

caccggtggt gatgctgatc aatatcccaa aggaaagcct accctaattg cctacgacct 480

caagaaggat catactccgg aaattcatcg atttgaaatt ccagacgatc tctatagctc 540

acaagttgaa tttggtggat ttgccgttga tgttgttaac acgaaaggag actgtacgga 600

gtcatttgtc tacctgacca atttcaagga taactctcta attgtctacg atgagacaca 660

aaagaaagct tggaaattca cagataaaac atttgaagct gataaggaat ccacgttctc 720

ctactcggga gaggaacaaa tgaagtacaa agtcggtctt tttgggatag ctctgggtga 780

tagggatgaa atggggcatc gtcctgcctg ctacatcgct gggagtagca ccaaagtcta 840

cagtgttaac actaaagaac tcaaaacaga gaatggtcag ttaaatcctc agcttcacgg 900

tgatcgtgga aagtacacag atgcaattgc cctagcctac gatcctgagc ataaagtcct 960

ctactttgct gaatccgaca gcaggcaggt gtcctgttgg aatgtaaata tggagctaaa 1020

accagacaat acggatgtga tcttctctag tgcccgtttt acttttggaa cggatatttt 1080

ggttgatagc aagggaatgc tgtggataat ggctaatgga catccaccag tagaggatca 1140

agagaagatt tggaagatga gattcgtaaa ccggaagatc cgtattatga aagtggatac 1200

ggaacgtgtt ttcaaatatt cacgctgcaa tccaaattat aagcccccaa aggaaattga 1260

agtttgagac acaggaaaaa gctcaatttt caacaagaat ttgatcttaa tctgaatacc 1320

ctaaagtctg tcaaagaatt tcatattatt tgaaaaccaa taaattgatt aattttccga 1380

aaaaaaaaaa aaaaaaaaaa aaaaaaaaa 1409

<210> 25
<211> 295
<212> PRT
<213> Lutzomyia longipalpis

<400> 25

Met Ile Lys Glu Val Phe Ser Leu Ala Leu Leu Val Ala Leu Ala Gln
1 5 10 15

Cys Ala Asn Glu Ile Pro Ile Asn Arg Gln Gly Lys Asp Tyr Pro Val
20 25 30

Pro Ile Ile Asp Pro Asn Lys Ser Ser Ser Asp Asp Tyr Phe Asp Asp
35 40 45

Arg Phe Tyr Pro Asp Ile Asp Asp Glu Gly Ile Ala Glu Ala Pro Lys
50 55 60

Asp Asn Arg Gly Lys Ser Arg Gly Gly Gly Ala Ala Gly Ala Arg Glu
65 70 75 80

Gly Arg Leu Gly Thr Asn Gly Ala Lys Pro Gly Gln Gly Gly Thr Arg
85 90 95

Pro Gly Gln Gly Gly Thr Arg Pro Gly Gln Gly Gly Thr Arg Pro Gly
100 105 110

Gln Gly Gly Thr Arg Pro Gly Gln Gly Gly Thr Arg Pro Gly Gln Gly
115 120 125

Arg Thr Lys Pro Ala Gln Gly Thr Thr Arg Pro Ala Gln Gly Thr Arg
130 135 140

Asn Pro Gly Ser Val Gly Thr Lys Glu Ala Gln Asp Ala Ser Lys Gln
145 150 155 160

Gly Gln Gly Lys Arg Arg Pro Gly Gln Val Gly Gly Lys Arg Pro Gly
165 170 175

Gln Ala Asn Ala Pro Asn Ala Gly Thr Arg Lys Gln Gln Lys Gly Ser
180 185 190

Arg Gly Val Gly Arg Pro Asp Leu Ser Arg Tyr Lys Asp Ala Pro Ala
195 200 205

Lys Phe Val Phe Lys Ser Pro Asp Phe Ser Gly Glu Gly Lys Thr Pro

210 215 220

Thr Val Asn Tyr Phe Arg Thr Lys Lys Lys Glu His Ile Val Thr Arg
225 230 235 240

Gly Ser Pro Asn Asp Glu Phe Val Leu Glu Ile Leu Asp Gly Asp Pro
245 250 255

Thr Gly Leu Gly Leu Lys Ser Glu Thr Ile Gly Lys Asp Thr Arg Leu
260 265 270

Val Leu Glu Asn Pro Asn Gly Asn Ser Ile Val Ala Arg Val Lys Ile
275 280 285

Tyr Lys Asn Gly Tyr Ser Gly
290 295

<210> 26
<211> 989
<212> DNA
<213> Lutzomyia longipalpis

<400> 26
actaaagcgt ctcaccgaaa tcagggaaaa tgattaagga agttttctct ctggctctac 60

ttgtggcctt ggcacagtgt gctaatgaaa tccctattaa tcgtcagggg aaagattatc 120

cagttccgat cattgatcca ataaaatcat cttcggatga ttatttcgat gatcgcttct 180

accctgatat tgatgatgag ggcatagctg aggctcctaa ggataatagg ggaaaatccc 240

gtggtggtgg tgcggctggc gcaagagaag gtaggttagg tacgaatggg gctaaaccgg 300

gtcagggtgg aactagacca ggacagggtg gaactaggcc aggacagggt ggaactaggc 360

caggtcaggg tggaactagg ccaggtcagg gtggaactag acctgggcaa ggtagaacta 420

agcctgctca gggaactact aggccagctc agggaactag aaatccagga tcggttggta 480

cgaaagaagc ccaggatgcg tcaaaacaag gtcaaggtaa aagaaggcca gggcaagttg 540

gtggtaaaag accaggacaa gcaaatgctc ctaatgcagg cactagaaag caacagaaag 600

gcagtagagg cgttggaagg cctgatctat cgcgctacaa agatgcccct gctaaattcg 660

ttttcaaatc tcccgatttc agtggagaag gcaaaactcc aactgtaaat tactttagaa 720

cgaagaagaa ggagcacatt gtgacccgtg gtagtcctaa tgatgaattt gttctggaga 780

ttctcgatgg ggatccaact gggcttggac taaagagtga aaccataggc aaagatacgc 840

gtttagtgct ggagaatcct aatggaaatt ccatcgtggc tcgtgttaag atctacaaga 900

acggttattc aggatgaaga agaaatcctt tgatttcccc ccccccctct tcctttaaaa 960

ttcaacataa taaaaaaaaa aaaaaaaaa 989

<210> 27
<211> 148
<212> PRT
<213> Lutzomyia longipalpis

<400> 27

Met Asn Ser Val Asn Thr Leu Ile Leu Thr Leu Leu Phe Ala Ile Phe
1 5 10 15

Leu Leu Val Lys Arg Ser Gln Ala Phe Leu Pro Ser Asp Pro Ser Ile
20 25 30

Cys Val Lys Asn Leu Val Leu Asp Thr Gly Arg Thr Cys Glu Glu Ser
35 40 45

Glu Tyr Phe Pro Asp Ile Lys Asn Val Lys Asn Gly Lys Arg Val Tyr
50 55 60

Ile Val Cys Thr Asp Ser Asp Ala Val Asp Tyr Lys Phe Tyr Ile Cys
65 70 75 80

Phe Asp Met Asn Arg Leu Ser Gly Pro Pro Tyr Pro Glu Glu Glu Ile
85 90 95

Leu Arg Glu Ser Thr Val Thr Tyr Ala Gln Ile Tyr Glu Leu Met Thr
100 105 110

Thr Glu Thr Thr Glu Thr Lys Lys Pro Lys Lys Lys Pro Lys Asn Ser
115 120 125

Lys Thr Asp Asp Pro Pro Ala Ile Arg Pro Gly Phe Ser Phe Arg Asn
130 135 140

Ser Ile Ser Val
145

<210> 28
<211> 826
<212> DNA
<213> Lutzomyia longipalpis

<400> 28
gtcttttcct gagtgtttca ttaacaaaat gaattcagta aacactttaa ttttaactct 60

tctatttgca attttttttat tagtgaaaag gtctcaggct tttcttccat ctgacccaag 120

tatctgtgtt aaaaatttag tattggatac aggaaggact tgtgaggaaa gtgaatattt 180

tccggatatc aagaacgtta aaaatggaaa aagagtttac attgtctgca ctgattcaga 240

tgcagttgat tataaatttt atatttgttt cgatatgaat cgtctttctg gaccaccgta 300

tcctgaggaa gaaatccttc gtgaatcaac ggtaacttat gcccaaattt atgagctgat 360

gactacggaa accactgaaa ccaaaaagcc aaaaaagaaa ccaaagaatt caaaaacgga 420

cccagaccct ccagcaattc gtccaggatt ttcatttaga aattcaattt ctgtttaatt 480

ttacaattta ttttgaaaga aaaatgatat ttcgaaatat tctatacaaa aaaacaacag 540

ttataaaacg aaaattcaat catttcaatg agaaaactta gtcttgagta aggtttattc 600

accacccgac gccacgctat ggtgaataat tttctttatt caccacatca aaatgacggc 660

ttataaactt caacaaatag tttggaaaat acatttctaa ctaatgcaat gtttacttaa 720

aatcacttta caaattcacg catttgagat gcaacaaata tatacaattc aacgatataa 780

actttccaca aggaaaactt tcaaccaaaa aaaaaaaaaa aaaaaa 826

<210> 29
<211> 397
<212> PRT
<213> Lutzomyia longipalpis

<400> 29

Met Lys Leu Phe Phe Phe Leu Tyr Thr Phe Gly Leu Val Gln Thr Ile
1 5 10 15

Phe Gly Val Glu Ile Lys Gln Gly Phe Lys Trp Asn Lys Ile Leu Tyr
20 25 30

Glu Gly Asp Thr Ser Glu Asn Phe Asn Pro Asp Asn Asn Ile Leu Thr
35 40 45

Ala Phe Ala Tyr Asp Pro Glu Ser Gln Lys Leu Phe Leu Thr Val Pro
50 55 60

Arg Lys Tyr Pro Glu Thr Met Tyr Thr Leu Ala Glu Val Asp Thr Glu
65 70 75 80

Lys Asn Ser Phe Glu Ser Gly Asp Thr Ser Pro Leu Leu Gly Lys Phe
85 90 95

Ser Gly His Glu Thr Gly Lys Glu Leu Thr Ser Val Tyr Gln Pro Val
100 105 110

Ile Asp Glu Cys His Arg Leu Trp Val Val Asp Val Gly Ser Val Glu
115 120 125

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Arg Asn Ser Asp Gly Thr Glu Gly Gln Pro Glu His Asn Pro Thr Leu
    130                 135                 140

Val Ala Tyr Asp Leu Lys Glu Ala Asn Tyr Pro Glu Val Ile Arg Tyr
145                 150                 155                 160

Thr Phe Pro Asp Asn Ser Ile Glu Lys Pro Thr Phe Leu Gly Gly Phe
                165                 170                 175

Ala Val Asp Val Val Lys Pro Asp Glu Cys Ser Glu Thr Phe Val Tyr
            180                 185                 190

Ile Thr Asn Phe Leu Thr Asn Ala Leu Ile Val Tyr Asp His Lys Asn
        195                 200                 205

Lys Asp Ser Trp Thr Val Gln Asp Ser Thr Phe Gly Pro Asp Lys Lys
    210                 215                 220

Ser Lys Phe Asp His Asp Gly Gln Gln Tyr Glu Tyr Glu Ala Gly Ile
225                 230                 235                 240

Phe Gly Ile Thr Leu Gly Glu Arg Asp Asn Glu Gly Asn Arg Gln Ala
                245                 250                 255

Tyr Tyr Leu Val Ala Ser Ser Thr Lys Leu His Ser Ile Asn Thr Lys
            260                 265                 270

Glu Leu Lys Gln Lys Gly Ser Lys Val Asn Ala Asn Tyr Leu Gly Asp
        275                 280                 285

Arg Gly Glu Ser Thr Asp Ala Ile Gly Leu Val Tyr Asp Pro Lys Thr
    290                 295                 300

Lys Thr Ile Phe Phe Val Glu Ser Asn Ser Lys Arg Val Ser Cys Trp
305                 310                 315                 320

Asn Thr Gln Glu Thr Leu Asn Lys Asp Lys Ile Asp Val Ile Tyr His
                325                 330                 335

Asn Ala Asp Phe Ser Phe Gly Thr Asp Ile Ser Ile Asp Ser Gln Asp
            340                 345                 350

Asn Leu Trp Phe Leu Ala Asn Gly Leu Pro Pro Leu Glu Asn Ser Asp
        355                 360                 365
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Lys Phe Val Phe Thr Lys Pro Arg Tyr Gln Ile Phe Lys Val Asn Ile
370 375 380

Gln Glu Ala Ile Ala Gly Thr Lys Cys Glu Lys Asn Leu
385 390 395

<210> 30
<211> 1325
<212> DNA
<213> Lutzomyia longipalpis

<400> 30
atcattcaaa aggcagcagc acaatgaagt tatttttctt tctttacact tttggtctag 60

tccaaacgat ttttggagta gaaattaaac aaggatttaa atggaataaa atcctttatg 120

agggcgatac atcagaaaac ttcaatccag ataacaacat ccttacggct tttgcgtacg 180

atcctgagag tcagaaactc ttcctaactg tcccgaggaa atatcccgaa actatgtaca 240

ctttggcaga agttgatact gagaaaaatt cttttgaatc gggagatact tccccgctcc 300

ttggaaaatt cagtggtcat gaaactggga aagaacttac atcagtttat cagccagtta 360

tcgatgaatg tcatcgtctt tgggttgttg atgttggatc agtagaacgt aactcagacg 420

gcacagaagg tcagccagaa cataatccta cccttgtggc gtacgatctc aaagaagcca 480

actatcctga agttattcgt tacacgtttc ccgataattc cattgagaag cccacatttc 540

tgggtggatt tgccgttgat gttgtaaagc cggatgaatg cagtgaaact tttgtctaca 600

tcacaaactt cctcaccaac gccctcatag tatacgatca taagaataag gactcctgga 660

agtatgaata cgaagcagga atcttcggga ttacccttgg agagagagat aacgaaggaa 780

atcgtcaagc gtactattta gtagcaagta gtaccaaact tcacagcatc aacaccaaag 840

aactgaagca aaaaggaagc aaagttaatg caaattattt gggagatcgt ggtgaatcca 900

ccgatgccat aggcttagtt tacgatccaa aaaccaaaac tatcttcttc gttgagtcaa 960

atagcaaaag agtatcatgc tggaataccc aggaaacact aaacaaggat aaaattgatg 1020

taatctatca caatgcagac ttttcctttg gaacagatat atcgattgat agtcaggata 1080

atttgtggtt cctagcaaat ggacttccac ctctggaaaa ttctgataaa tttgtcttta 1140

caaagccacg ttatcaaata ttcaaagtca acattcaaga agcaattgct ggaactaaat 1200

gtgaaaagaa tctttaacaa atgaaacttt gtagaaaaat acataatatc tgaataaaaa 1260

gtcataaatg taccataaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1320

aaaaa 1325

<210> 31
<211> 350
<212> PRT
<213> Lutzomyia longipalpis

<400> 31

Met Thr Phe Leu Ile Ile Leu Gly Ala Phe Leu Leu Val Gln Ile Ile
1 5 10 15

Thr Ala Ser Ala Leu Gly Leu Pro Glu Gln Phe Lys Gly Leu Glu Asp
20 25 30

Leu Pro Lys Lys Pro Leu Ala Glu Thr Tyr Tyr His Glu Gly Leu Asn
35 40 45

Asp Gly Lys Thr Asp Glu Met Val Asp Ile Phe Lys Ser Leu Ser Asp
50 55 60

Glu Phe Lys Phe Ser Asp Glu Asn Leu Asp Val Gly Glu Glu Lys Asn
65 70 75 80

Tyr Lys Lys Arg Asp Ile Thr Gln Asn Ser Val Ala Arg Asn Phe Leu
85 90 95

Ser Asn Val Lys Gly Ile Pro Ser Met Pro Ser Leu Pro Ser Met Pro
100 105 110

Ser Met Pro Ser Ile Pro Ser Leu Trp Ser Ser Gln Thr Gln Ala Ala
115 120 125

Pro Asn Thr Ala Leu Ala Leu Pro Glu Ser Asp Tyr Ser Leu Leu Asp
130 135 140

Met Pro Asn Ile Val Lys Asn Phe Leu Lys Glu Thr Arg Asp Leu Tyr
145 150 155 160

Asn Asp Val Gly Ala Phe Leu Lys Ala Ile Thr Glu Ala Leu Thr Asn
165 170 175

Arg Ser Ser Ser Ser Gln Leu Leu Ser Ser Pro Met Val Ser Thr Asn
180 185 190

Lys Thr Lys Glu Phe Ile Arg Asn Glu Ile Gln Lys Val Arg Lys Val
195 200 205

Arg Asn Phe Val Gln Glu Thr Leu Gln Lys Ile Arg Asp Ile Ser Ala
210 215 220

Ala Ile Ala Lys Lys Val Lys Ser Ser Glu Cys Leu Ser Asn Leu Thr
225 230 235 240

Asp Ile Lys Gly Leu Val Ser Asp Gly Ile Asn Cys Leu Lys Glu Lys
245 250 255

Phe Asn Asp Gly Lys Arg Ile Ile Leu Gln Leu Tyr Asn Asn Leu Leu
260 265 270

Lys Gly Leu Lys Ile Pro Asn Asp Leu Met Val Glu Leu Lys Lys Cys
275 280 285

Asp Thr Asn Gln Asn Asn Thr Leu Gly Arg Ile Ile Cys Tyr Phe Leu
290 295 300

Thr Pro Leu Gln Leu Glu Lys Glu Gln Ile Leu Leu Pro Val Glu Phe
305 310 315 320

Ile Lys Arg Ile Leu Glu Leu Thr His Tyr Phe Ser Thr Met Lys Glu
325 330 335

Asp Leu Ile Asn Cys Gly Ile Thr Thr Ile Ala Ser Ile Thr
340 345 350

<210> 32
<211> 1275
<212> DNA
<213> Lutzomyia longipalpis

<400> 32
ctttaaagca aaaattttgt gggaaaggaa gttacccgga gatgacgttt ctaattatac 60

ttggtgcatt tctccttgtt caaattatta cagcttcagc tttaggattg cctgaacagt 120

ttaaaggttt agaggattta cctaaaaaac ctttggcaga gacttattat cacgaaggat 180

tgaatgatgg aaaaacggat gaaatggtgg atatttttaa aagtcttagc gatgaattta 240

aattcagtga tgaaaattta gatgttggtg aggagaaaaa ttacaagaaa cgtgatataa 300

cccaaaattc agtggcaagg aacttcctat caaacgtaaa gggaattcct tcaatgccat 360

cactcccttc aatgccttca atgccatcaa ttccttcact ttggtcaagt cagacacagg 420

cggcaccaaa taccgcactt gcccttcctg aatctgatta ttccccttcta gatatgccga 480

atattgtgaa aaatttccta aaggaaacaa gagacctcta taacgatgtt ggagcttttc 540

ttaaggcaat tacagaagct ttaacaaata gatcttcatc atctcaactt ctttcctccc 600

caatggtgag cacgaataaa accaaagaat ttattcggaa tgaaatacaa aaagtccgaa 660

aagtgagaaa tttcgtccag gaaactcttc agaaaatccg agacatttct gctgctattg 720

ccaaaaaggt aaaatcatca gaatgtctgt ccaatcttac ggacatcaaa ggacttgtat 780

cagacggaat taattgttta aaggaaaaat tcaatgatgg aaaacgaatt atcctgcaat 840

tgtacaataa tttactaaaa ggactcaaaa ttccaaatga cctaatggtt gaattgaaga 900

aatgtgatac aaatcaaaac aatactttgg gaagaataat ctgttatttt ttgacaccat 960

tgcaactgga aaaagaacaa attcttctac ctgtagaatt tataaagcgc attcttgaat 1020

taacccacta cttttccaca atgaaagaag atcttatcaa ctgtggcatc acaacgattg 1080

catccattac gtaaaaaatg gaaaaatgtg ccggtgaaat gcttgaaatc accaaagaaa 1140

tttcatcgca aataacagtt ccagaataac caaattttaa tgattacttc tcaaggaaaa 1200

tactaccaaa aggcattaat taaaacgatg ttttttataa acaatgtaag aaaaaaaaaa 1260

aaaaaaaaaa aaaaa 1275

<210> 33
<211> 60
<212> PRT
<213> Lutzomyia longipalpis

<400> 33

Met Leu Lys Ile Val Leu Phe Leu Ser Val Leu Ala Val Leu Val Ile
1 5 10 15

Cys Val Ala Ala Met Pro Gly Ser Asn Val Pro Trp His Ile Ser Arg
20 25 30

Glu Glu Leu Glu Lys Leu Arg Glu Ala Arg Lys Asn His Lys Ala Leu
35 40 45

Glu Lys Ala Ile Asp Glu Leu Ile Asp Lys Tyr Leu
50 55 60

<210> 34
<211> 413
<212> DNA
<213> Lutzomyia longipalpis

<400> 34
agttaatctt ctgtcaagct acaaaaatgc ttaaaatcgt tttatttcta tcagttttgg 60

ctgtattagt gatttgtgta gcagcaatgc caggatccaa tgttccttgg cacatttcac 120

gagaagagct tgagaagctt cgtgaagctc gaaagaatca caaggcactc gagaaggcaa 180

ttgatgaatt aattgacaaa tatctctgat tttgaagagc aaggaagagg aaataaacgg 240

ccgaggaagg attttcttta gagattcttc tttttattac ttcaaaccta acttcaaaat 300

cagtctgata ttttttttaat ttgaaaaaaa tattgaaaat tttaactatt tgtgaaattt 360

aaataaataa agaatgtcag aagcaaaaaa aaaaaaaaaa aaaaaaaaaa aaa 413

<210> 35
<211> 120
<212> PRT
<213> Lutzomyia longipalpis

<400> 35

Met Lys Phe Ser Cys Pro Val Phe Val Ala Ile Phe Leu Leu Cys Gly
1 5 10 15

Phe Tyr Arg Val Glu Gly Ser Ser Gln Cys Glu Glu Asp Leu Lys Glu
20 25 30

Glu Ala Glu Ala Phe Phe Lys Asp Cys Asn Glu Ala Lys Ala Asn Pro
35 40 45

Gly Glu Tyr Glu Asn Leu Thr Lys Glu Glu Met Phe Glu Glu Leu Lys
50 55 60

Glu Tyr Gly Val Ala Asp Thr Asp Met Glu Thr Val Tyr Lys Leu Val
65 70 75 80

Glu Glu Cys Trp Asn Glu Leu Thr Thr Thr Asp Cys Lys Arg Phe Leu
85 90 95

Glu Glu Ala Glu Cys Phe Lys Lys Lys Asn Ile Cys Lys Tyr Phe Pro
100 105 110

Asp Glu Val Lys Leu Lys Lys Lys
115 120

<210> 36
<211> 428
<212> DNA
<213> Lutzomyia longipalpis

<400> 36
aattttcacc atgaagtttt cttgcccagt tttcgttgca attttccttt tgtgcggatt 60

ttatcgtgtt gaggggtcat cacaatgtga agaagattta aaagaagaag ctgaagcttt 120

ctttaaggat tgcaatgaag caaaagccaa tcctggtgaa tacgagaatc tcaccaaaga 180

agaaatgttt gaagaattga aagaatatgg agttgctgac acagacatgg agacagttta 240

caaacttgtg gaagaatgtt ggaatgaatt aacaacaacg gattgtaaga gatttctcga 300

agaggctgaa tgcttcaaga agaagaatat ttgtaaatat ttcccagatg aagtgaaatt 360

gaagaagaaa taaattttta gcttgaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 420

aaaaaaaa 428

<210> 37
<211> 572
<212> PRT
<213> Lutzomyia longipalpis

<400> 37

Met Leu Phe Phe Leu Asn Phe Phe Val Leu Val Phe Ser Ile Glu Leu
1 5 10 15

Ala Leu Leu Thr Ala Ser Ala Ala Ala Glu Asp Gly Ser Tyr Glu Ile
20 25 30

Ile Ile Leu His Thr Asn Asp Met His Ala Arg Phe Asp Gln Thr Asn
35 40 45

Ala Gly Ser Asn Lys Cys Gln Glu Lys Asp Lys Ile Ala Ser Lys Cys
50 55 60

Tyr Gly Gly Phe Ala Arg Val Ser Thr Met Val Lys Lys Phe Arg Glu
65 70 75 80

Glu Asn Gly Ser Ser Val Leu Phe Leu Asn Ala Gly Asp Thr Tyr Thr
85 90 95

Gly Thr Pro Trp Phe Thr Leu Tyr Lys Glu Thr Ile Ala Thr Glu Met
100 105 110

Met Asn Ile Leu Arg Pro Asp Ala Ala Ser Leu Gly Asn His Glu Phe
115 120 125

Asp Lys Gly Val Glu Gly Leu Val Pro Phe Leu Asn Gly Val Thr Phe
130 135 140

Pro Ile Leu Thr Ala Asn Leu Asp Thr Ser Gln Glu Pro Thr Met Thr
145 150 155 160

Asn Ala Lys Asn Leu Lys Arg Ser Met Ile Phe Thr Val Ser Gly His
165 170 175

Arg Val Gly Val Ile Gly Tyr Leu Thr Pro Asp Thr Lys Phe Leu Ser
180 185 190

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Asp Val Gly Lys Val Asn Phe Ile Pro Glu Val Glu Ala Ile Asn Thr
        195                 200                 205

Glu Ala Gln Arg Leu Lys Lys Glu Glu Asn Ala Glu Ile Ile Ile Val
    210                 215                 220

Val Gly His Ser Gly Leu Ile Lys Asp Arg Glu Ile Ala Glu Lys Cys
225                 230                 235                 240

Pro Leu Val Asp Ile Ile Val Gly Gly His Ser His Thr Phe Leu Tyr
                245                 250                 255

Thr Gly Ser Gln Pro Asp Arg Glu Val Pro Val Asp Val Tyr Pro Val
            260                 265                 270

Val Val Thr Gln Ser Ser Gly Lys Lys Val Pro Ile Val Gln Ala Tyr
        275                 280                 285

Cys Phe Thr Lys Tyr Leu Gly Tyr Phe Lys Val Thr Ile Asn Gly Lys
    290                 295                 300

Gly Asn Val Val Gly Trp Thr Gly Gln Pro Ile Leu Leu Asn Asn Asn
305                 310                 315                 320

Ile Pro Gln Asp Gln Glu Val Leu Thr Ala Leu Glu Lys Tyr Arg Glu
                325                 330                 335

Arg Val Glu Asn Tyr Gly Asn Arg Val Ile Gly Val Ser Arg Val Ile
            340                 345                 350

Leu Asn Gly Gly His Thr Glu Cys Arg Phe His Glu Cys Asn Met Gly
        355                 360                 365

Asn Leu Ile Thr Asp Ala Phe Val Tyr Ala Asn Val Ile Ser Thr Pro
    370                 375                 380

Met Ser Thr Asn Ala Trp Thr Asp Ala Ser Val Val Leu Tyr Gln Ser
385                 390                 395                 400

Gly Gly Ile Arg Ala Pro Ile Asp Pro Arg Thr Ala Ala Gly Ser Ile
                405                 410                 415

Thr Arg Leu Glu Leu Asp Asn Val Leu Pro Phe Gly Asn Ala Leu Tyr
            420                 425                 430
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Val Val Lys Val Pro Gly Asn Val Leu Arg Lys Ala Leu Glu His Ser
435 440 445

Val His Arg Tyr Ser Asn Thr Ser Gly Trp Gly Glu Phe Pro Gln Val
450 455 460

Ser Gly Leu Lys Ile Arg Phe Asn Val Asn Glu Glu Ile Gly Lys Arg

Val Lys Ser Val Lys Val Leu Cys Ser Asn Cys Ser Gln Pro Glu Tyr
485 490 495

Gln Pro Leu Arg Asn Lys Lys Thr Tyr Asn Val Ile Met Asp Ser Phe
500 505 510

Met Lys Asp Gly Gly Asp Gly Tyr Ser Met Phe Lys Pro Leu Lys Ile
515 520 525

Ile Lys Thr Leu Pro Leu Gly Asp Ile Glu Thr Val Glu Ala Tyr Ile
530 535 540

Glu Lys Met Gly Pro Ile Phe Pro Ala Val Glu Gly Arg Ile Thr Val
545 550 555 560

Leu Gly Gly Leu Gln Lys Ser Asp Glu Asp Trp His
565 570

<210> 38
<211> 1839
<212> DNA
<213> Lutzomyia longipalpis

<400> 38
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agatcataat tcttcacacc aatgatatgc acgcgcgttt tgatcaaacc aatgctggaa 180

gcaacaaatg ccaagaaaaa gacaagattg cttccaaatg ctacggagga tttgcaagag 240

tttcaacaat ggtgaaaaaa ttccgagaag aaaatggcag cagtgtcttg ttcttgaatg 300

ctggtgacac gtatacaggt accccatggt ttaccctcta caaggagacc attgcaacgg 360

agatgatgaa catccttcgt ccagatgcag cctcactggg aaatcatgaa ttcgacaaag 420

gagtagaagg actcgtgcca ttcctcaatg gtgtcacctt ccctatttta acagcgaatt 480

tggacacttc tcaagagcca acaatgacca atgctaaaaa tctcaaacgc tcaatgattt 540

ttacggtttc cgggcacaga gttggtgtaa ttggctacct aacgcctgat acaaaattcc 600

tctcggacgt tggtaaagtt aattttattc cggaagttga agccatcaat acggaagcac 660

agcgtctgaa gaaagaggaa aatgccgaaa taatcatcgt tgttggacat tcagggttga 720

taaaagatcg agaaattgca gagaaatgcc cactggttga cataattgtt ggaggacatt 780

cacacacatt cctctacaca ggaagtcagc ctgatcgtga ggttcctgta gacgtttatc 840

ctgttgttgt gacccaatcc agtgggaaga aagttccaat tgttcaagcc tattgcttta 900

caaagtattt ggggtacttt aaagtgacga tcaacggaaa aggaaatgtt gtgggatgga 960

ctgggcagcc aattctcctt aataacaaca ttccccaaga tcaggaagtt ctcactgctc 1020

ttgaaaagta cagagaacgc gtggaaaact atggaaatcg cgtaattgga gtttcccgtg 1080

taattctcaa tgggggggcat actgaatgtc gtttccatga atgcaatatg ggtaatctca 1140

tcacggacgc ttttgtgtat gccaatgtaa tcagtacacc aatgagtacg aatgcctgga 1200

cagatgcaag tgttgttctg tatcaaagtg gtggcattcg tgccccaatt gatcctcgta 1260

ccgcggcagg gagcatcaca cgcctcgagt tggacaatgt tctaccattt gggaatgcac 1320

tgtacgtcgt aaaagttcct gggaatgtct tacgcaaagc tttggaacat tcagttcatc 1380

gatactccaa cacttcggga tggggagaat ttccacaagt ttcggggcta aagattcgtt 1440

ttaacgtcaa tgaagaaatt ggaaaacgcg taaagtccgt taaagttctc tgtagcaatt 1500

gctctcaacc tgaataccaa ccactgagaa ataaaaaaac ttacaacgtt atcatggaca 1560

gttttatgaa ggatggaggt gatgggtata gcatgttcaa gcccttgaag atcatcaaga 1620

ccctcccact gggagatatt gaaacagtag aagcttatat tgagaaaatg ggccccattt 1680

tcccagcagt cgagggaagg atcactgttc ttgggggact tcaaaaatca gatgaggatt 1740

ggcattagaa acatcctgga cgttatggaa agaataaaag aaggatcata gaaaaaaaaa 1800

aaaaaaaaat aaaaaaaaaa aaaaaaaaaa aaaaaaaaa 1839

<210> 39
<211> 86
<212> PRT
<213> Lutzomyia longipalpis

<400> 39

Met Lys Gln Ile Leu Leu Ile Ser Leu Val Val Ile Leu Ala Val Leu
1 5 10 15

Ala Phe Asn Val Ala Glu Gly Cys Asp Ala Thr Cys Gln Phe Arg Lys
20 25 30

Ala Ile Glu Asp Cys Lys Lys Lys Ala Asp Asn Ser Asp Val Leu Gln
35 40 45

Thr Ser Val Gln Thr Thr Ala Thr Phe Thr Ser Met Asp Thr Ser Gln
50 55 60

Leu Pro Gly Asn Asn Val Phe Lys Ala Cys Met Lys Glu Lys Ala Lys
65 70 75 80

Glu Phe Arg Ala Gly Lys
85

<210> 40
<211> 419
<212> DNA
<213> Lutzomyia longipalpis

<400> 40
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tcttgccgtg cttgccttca atgttgctga gggctgtgat gcaacatgcc aatttcgcaa 120

agccatagaa gactgcaaga agaaggcgga taatagcgat gttttgcaga cttctgtaca 180

aacaactgca acattcacat caatggatac atcccaacta cctggaaata atgtcttcaa 240

agcatgcatg aaggagaagg ctaaggaatt tagggcagga aagtaagaga ttgaggaaaa 300

ttgtagccga agagagaagg aaggaaagtc ccatattttg tttgttaatt gtaacgaatt 360

ttgcgaaaaa aataaaatat tatgcactcc aaaaaaaaaa aaaaaaaaaa aaaaaaaaa 419

<210> 41
<211> 84
<212> PRT
<213> Lutzomyia longipalpis

<400> 41

Met Asn Val Leu Phe Val Ser Phe Thr Leu Thr Ile Leu Leu Leu Cys
1 5 10 15

Val Lys Ala Arg Pro Glu Asp Phe Val Ala Leu Gln Asp Gln Ala Asn
20 25 30

Phe Gln Lys Cys Leu Glu Gln Tyr Pro Glu Pro Asn Gln Ser Gly Glu
35 40 45

Val Leu Ala Cys Leu Lys Lys Arg Glu Gly Ala Lys Asp Phe Arg Glu
50 55 60

Lys Arg Ser Leu Asp Asp Ile Glu Gly Thr Phe Gln Glu Ser Gly Asn
65 70 75 80

Leu Trp Gly Ala

<210> 42
<211> 429
<212> DNA
<213> Lutzomyia longipalpis

<400> 42
tatttttaat aattctgtgt aaaatgaacg ttcttttcgt gtctttcacg ctcacaattc 60

ttcttctctg tgttaaggca cggccagaag atttcgtagc tcttcaggat caagctaatt 120

tccagaaatg cctcgaacaa tatccagaac caaatcaatc tggagaagtt cttgcgtgcc 180

tcaagaagcg cgaaggtgcc aaagatttcc gggaaaagag gagcctggat gacatagaag 240

ggactttcca agagtctgga aatctctggg gtgcatagga agctcagagg acttctaatc 300

aatctgtgag aagagaaccc aacggctaga gaaaatttaa ggaaaataaa gaaattaatg 360

aagcattaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 420

aaaaaaaaa 429

<210> 43
<211> 626
<212> PRT
<213> Lutzomyia longipalpis

<400> 43

Met Lys Ile Thr Val Ile Leu Phe Thr Gly Phe Thr Ile Ala Leu Val
1 5 10 15

Ser Ser Ala Val Leu Lys Lys Asn Gly Glu Thr Ile Glu Glu Glu Glu
20 25 30

Val Arg Ala Glu Gln Arg Leu Arg Glu Ile Asn Glu Glu Leu Asp Arg
35 40 45

Arg Lys Asn Ile Asn Thr Val Ala Ala Trp Ala Tyr Ala Ser Asn Ile
50 55 60

Thr Glu Val Asn Leu Lys Asn Met Asn Asp Val Ser Val Glu Thr Ala
65 70 75 80

Lys Tyr Tyr Lys Glu Leu Ala Ser Glu Leu Lys Gly Phe Asn Ala Lys
85 90 95

Glu Tyr Lys Ser Glu Asp Leu Lys Arg Gln Ile Lys Lys Leu Ser Lys
100 105 110

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Leu Gly Tyr Ser Ala Leu Pro Ser Glu Lys Tyr Lys Glu Leu Leu Glu
        115                 120                 125

Ala Ile Thr Trp Met Glu Ser Asn Tyr Ala Lys Val Lys Val Cys Ser
    130                 135                 140

Tyr Lys Asp Pro Lys Lys Cys Asp Leu Ala Leu Glu Pro Glu Ile Thr
145                 150                 155                 160

Glu Ile Leu Ile Lys Ser Arg Asp Pro Glu Glu Leu Lys Tyr Tyr Trp
                165                 170                 175

Lys Gln Trp Tyr Asp Lys Ala Gly Thr Pro Thr Arg Glu Ser Phe Asn
            180                 185                 190

Lys Tyr Val Gln Leu Asn Arg Glu Ala Ala Lys Leu Asp Gly Phe Tyr
        195                 200                 205

Ser Gly Ala Glu Ser Trp Leu Asp Glu Tyr Glu Asp Glu Thr Phe Glu
    210                 215                 220

Lys Gln Leu Glu Asp Ile Phe Ala Gln Ile Arg Pro Leu Tyr Glu Gln
225                 230                 235                 240

Leu His Ala Tyr Val Arg Phe Lys Leu Arg Glu Lys Tyr Gly Asn Asp
                245                 250                 255

Val Val Ser Glu Lys Gly Pro Ile Pro Met His Leu Leu Gly Asn Met
            260                 265                 270

Trp Gly Gln Thr Trp Ser Glu Val Ala Pro Ile Leu Val Pro Tyr Pro
        275                 280                 285

Glu Lys Lys Leu Leu Asp Val Thr Asp Glu Met Val Lys Gln Gly Tyr
    290                 295                 300

Thr Pro Ile Ser Met Phe Glu Lys Gly Asp Glu Phe Phe Gln Ser Leu
305                 310                 315                 320

Asn Met Thr Lys Leu Pro Lys Thr Phe Trp Glu Tyr Ser Ile Leu Glu
                325                 330                 335

Lys Pro Gln Asp Gly Arg Glu Leu Ile Cys His Ala Ser Ala Trp Asp
            340                 345                 350
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Phe Tyr Thr Lys Asp Asp Val Arg Lys Gln Cys Thr Arg Val Thr Met
355 360 365

Asp Gln Phe Phe Thr Ala His His Glu Leu Gly His Ile Gln Tyr Tyr
370 375 380

Leu Gln Tyr Gln His Leu Pro Ser Val Tyr Arg Glu Gly Ala Asn Pro
385 390 395 400

Gly Phe His Glu Ala Val Gly Asp Val Leu Ser Leu Ser Val Ser Ser
405 410 415

Pro Lys His Leu Glu Lys Val Gly Leu Leu Lys Asp Phe Lys Phe Asp
420 425 430

Glu Glu Ser Gln Ile Asn Gln Leu Leu Asn Leu Ala Leu Asp Lys Met
435 440 445

Ala Phe Leu Pro Phe Ala Tyr Thr Ile Asp Lys Tyr Arg Trp Gly Val
450 455 460

Phe Arg Gly Glu Ile Ser Pro Ser Glu Tyr Asn Cys Lys Phe Trp Glu
465 470 475 480

Met Arg Ser Tyr Tyr Gly Gly Ile Glu Pro Pro Ile Ala Arg Ser Glu
485 490 495

Ser Asp Phe Asp Pro Pro Ala Lys Tyr His Ile Ser Ser Asp Val Glu
500 505 510

Tyr Leu Arg Tyr Leu Val Ser Phe Ile Ile Gln Phe Gln Phe His Gln
515 520 525

Ala Val Cys Gln Lys Thr Gly Gln Phe Val Pro Asn Asp Pro Glu Lys
530 535 540

Thr Leu Leu Asn Cys Asp Ile Tyr Gln Ser Ala Glu Ala Gly Asn Ala
545 550 555 560

Phe Lys Glu Met Leu Lys Leu Gly Ser Ser Lys Pro Trp Pro Asp Ala
565 570 575

Met Glu Ile Leu Thr Gly Gln Arg Lys Met Asp Ala Ser Ala Leu Ile
580 585 590

Glu Tyr Phe Arg Pro Leu Ser Glu Trp Leu Gln Lys Lys Asn Lys Glu
595 600 605

Leu Gly Ala Tyr Val Gly Trp Asp Lys Ser Thr Lys Cys Val Lys Asn
610 615 620

Val Ser
625

<210> 44
<211> 2121
<212> DNA
<213> Lutzomyia longipalpis

<400> 44
gtatatcaag tatcattcaa gtgaatcatt ggctccgtaa tttgtacaaa agaaaaaaaa 60

gagtagtgct gtgcttaaga aaaacggtga aactattgaa gaagaagaag taagagctga 180

gcaacgactt agagagatca atgaggaact tgatcgtagg aagaatatca atactgtagc 240

cgcttgggct tatgcatcca atattactga ggtcaatctc aagaacatga atgatgtgtc 300

ggttgaaacc gcgaaatact acaaggaact tgcatctgaa ttgaagggat tcaatgccaa 360

ggaatacaag agtgaggatc tgaagagaca aattaagaag ctaagcaagt tgggatatag 420

tgctttacca tctgagaagt ataaggagct tttggaagct atcacatgga tggaatcgaa 480

ttatgcaaaa gtgaaagttt gctcatacaa ggatccaaag aaatgtgatt tagcacttga 540

acctgaaatt acggaaatcc ttattaaaag tcgagatcct gaggaactta aatattattg 600

gaaacaatgg tacgacaaag ctggcacacc aactcgagag agttttaata agtatgtaca 660

actaaatcgt gaagcagcga aattggatgg attttattcg ggtgcagaat cttggcttga 720

tgaatatgaa gatgagacat ttgagaaaca acttgaggat atcttcgccc aaattcgccc 780

actgtacgag caactccatg cttatgttag attcaagctg agggaaaagt atggaaatga 840

cgttgtttcg gagaaaggtc ccattccaat gcatctcttg gggaacatgt ggggtcaaac 900

gtggagtgaa gttgccccaa ttttagtccc ataccccgaa aagaagctcc tcgatgttac 960

cgatgagatg gttaagcagg gatacacacc aatttctatg tttgaaaaag gagacgaatt 1020

tttccaaagc ttgaatatga cgaaacttcc aaaaaccttc tgggagtaca gtattttgga 1080

aaaaccccaa gatggtaggg aattgatctg ccatgcaagt gcatgggact tctatacaaa 1140

ggatgatgta aggattaaac agtgtaccag agttacaatg gatcaattct tcacggctca 1200

tcatgagctt ggtcacattc aatattattt gcaatatcaa catttgccga gtgtttacag 1260

agaaggtgcc aatccaggct ttcacgaggc tgttggggat gttctctctc tttcggtatc 1320

aagtcctaaa catttggaaa aagttggttt gcttaaagac ttcaaatttg atgaagaatc 1380

ccagataaat caacttctaa atttagctct ggataaaatg gcattcctcc catttgccta 1440

taccattgat aaatatcgct ggggtgtgtt tcggggtgaa atttcgccgt ctgagtacaa 1500

ttgcaaattt tgggaaatgc gttcctacta tggtggtata gaaccaccaa ttgcacgttc 1560

tgagagtgat tttgatccac cagcaaaata tcatatttca tcggatgttg agtacctcag 1620

gtatttggtt tccttcatta ttcagttcca attccatcaa gctgtgtgcc aaaagactgg 1680

tcagttcgta ccgaatgatc cggagaagac tcttctaaat tgtgacatct accagagtgc 1740

tgaggctggt aatgccttca aagaaatgct caaattggga tcctcaaaac catggccaga 1800

tgcaatggaa attcttacgg ggcaaaggaa aatggatgct tctgcattaa ttgagtactt 1860

ccgtccactc agtgagtggt tgcagaagaa gaataaggaa ctaggagctt atgttggctg 1920

ggacaaatct actaagtgtg tcaaaaacgt cagttaattt tttgtgagcc ctaaaaaata 1980

ttcataacat ttcaatatga caaaatatat gattttcgtg aaaactaagc atgagtaagt 2040

ttttttttgtg aatttttagc agtttcattt cagaataaac gtcaaatttt taaaaaaaaa 2100

aaaaaaaaaa aaaaaaaaaa a 2121

<210> 45
<211> 42
<212> PRT
<213> Lutzomyia longipalpis

<400> 45

Met Lys Thr Phe Ala Leu Ile Phe Leu Ala Leu Ala Val Phe Val Leu
1 5 10 15

Cys Ile Asp Gly Ala Pro Thr Phe Val Asn Leu Leu Asp Asp Val Gln
20 25 30

Glu Glu Val Glu Val Asn Thr Tyr Glu Pro
35 40

<210> 46
<211> 463
<212> DNA
<213> Lutzomyia longipalpis

<400> 46
tcagttagtt gactaacaaa ccacaataga gacactaaaa tgaagacatt cgccttaatc 60

ttcttggctc ttgctgtttt tgtgctctgc attgacggag ctccaacttt tgtgaattta 120

ctggacgacg tacaggaaga ggtagaagtt aatacgtatg agccttagga agaaaatgtt 180

tgaggagttt caggcagagg cagagctttc ccagagaggg agcttttgcc ttgctgtaga 240

ttttttaaaaa tgaatcaatt tgattggagc aattacgcta tatttgtggg aatatttttg 300

aattaaaaac taattatgga aattaatata taatttttcag aatttcaata aattcatcaa 360

aattgtatta attaaaaaat attgtatgaa attcccaata aaagctttca aattaaaaaa 420

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaa 463

<210> 47
<211> 139
<212> PRT
<213> Lutzomyia longipalpis

<400> 47

Met Asn His Leu Cys Phe Ile Ile Ile Ala Leu Phe Phe Leu Val Gln
1 5 10 15

Gln Ser Leu Ala Glu His Pro Glu Glu Lys Cys Ile Arg Glu Leu Ala
20 25 30

Arg Thr Asp Glu Asn Cys Ile Leu His Cys Thr Tyr Ser Tyr Tyr Gly
35 40 45

Phe Val Asp Lys Asn Phe Arg Ile Ala Lys Lys His Val Gln Lys Phe
50 55 60

Lys Lys Ile Leu Val Thr Phe Gly Ala Val Pro Lys Lys Glu Lys Lys
65 70 75 80

Lys Leu Leu Glu His Ile Glu Ala Cys Ala Asp Ser Ala Asn Ala Asp
85 90 95

Gln Pro Gln Thr Lys Asp Glu Lys Cys Thr Lys Ile Asn Lys Tyr Tyr
100 105 110

Arg Cys Val Val Asp Gly Lys Ile Leu Pro Trp Asn Ser Tyr Ala Asp
115 120 125

Ala Ile Ile Lys Phe Asp Lys Thr Leu Asn Val
130 135

<210> 48
<211> 579
<212> DNA
<213> Lutzomyia longipalpis

<400> 48
ggccattatg gccggggata gaacttaatt gttgttaaaa tgaatcactt gtgctttatt 60

attattgctc tattcttttt ggttcaacaa tctttggctg aacatccaga agaaaaatgt 120

attagagaat tggcgagaac tgatgaaaac tgcattcttc attgtacgta ttcgtactac 180

ggattcgttg ataaaaattt caggatcgct aaaaaacatg ttcaaaaatt caaaaaaatc 240

ctagttacat tcggcgctgt tcctaagaaa gaaaaaaaga aacttttaga gcacattgag 300

gcttgtgcgg attctgcgaa tgctgatcaa cctcaaacta aagatgaaaa atgtacaaaa 360

ataaataagt actatcgttg tgttgtggat ggaaaaatat taccctggaa tagttatgct 420

gatgcaatca ttaagtttga taaaaccctt aacgtatgaa gcaaagatat tcgaaaaaaa 480

aacatcaaga ttatgctgga aagaaaaaaa taaaaaaaaa ttgtgctaat caaattgaat 540

taacgcttaa tgctatatta aaaaaaaaaa aaaaaaaaa 579

<210> 49
<211> 446
<212> PRT
<213> Lutzomyia longipalpis

<400> 49

Met Lys Ile Ile Phe Leu Ala Ala Phe Leu Leu Ala Asp Gly Ile Trp
1 5 10 15

Ala Ala Glu Glu Pro Ser Val Glu Ile Val Thr Pro Gln Ser Val Arg
20 25 30

Arg His Ala Thr Pro Lys Ala Gln Asp Ala Arg Val Gly Ser Glu Ser
35 40 45

Ala Thr Thr Ala Pro Arg Pro Ser Glu Ser Met Asp Tyr Trp Glu Asn
50 55 60

Asp Asp Phe Val Pro Phe Glu Gly Pro Phe Lys Asp Ile Gly Glu Phe
65 70 75 80

Asp Trp Asn Leu Ser Lys Ile Val Phe Glu Glu Asn Lys Gly Asn Ala
85 90 95

Ile Leu Ser Pro Leu Ser Val Lys Leu Leu Met Ser Leu Leu Phe Glu
100 105 110

Ala Ser Ala Ser Gly Thr Leu Thr Gln His Gln Leu Arg Gln Ala Thr
115 120 125

Pro Thr Ile Val Thr His Tyr Gln Ser Arg Glu Phe Tyr Lys Asn Ile
130 135 140

Phe Asp Gly Leu Lys Lys Lys Ser Asn Asp Tyr Thr Val His Phe Gly
145 150 155 160

Thr Arg Ile Tyr Val Asp Gln Phe Val Thr Pro Arg Gln Arg Tyr Ala
165 170 175

Ala Ile Leu Glu Lys His Tyr Leu Thr Asp Leu Lys Val Glu Asp Phe
180 185 190

Ser Lys Ala Lys Glu Thr Thr Gln Ala Ile Asn Ser Trp Val Ser Asn
195 200 205

Ile Thr Asn Glu His Ile Lys Asp Leu Val Lys Glu Glu Asp Val Gln
210 215 220

Asn Ser Val Met Leu Met Leu Asn Ala Val Tyr Phe Arg Gly Leu Trp
225 230 235 240

Arg Lys Pro Phe Asn Arg Thr Leu Pro Leu Pro Phe His Val Ser Ala
245 250 255

Asp Glu Ser Lys Thr Thr Asp Phe Met Leu Thr Asp Gly Leu Tyr Tyr
260 265 270

Phe Tyr Glu Ala Lys Glu Leu Asp Ala Lys Ile Leu Arg Ile Pro Tyr
275 280 285

Lys Gly Lys Gln Tyr Ala Met Thr Val Ile Leu Pro Asn Ser Lys Ser
290 295 300

Gly Ile Asp Ser Phe Val Arg Gln Ile Asn Thr Val Leu Leu His Arg
305 310 315 320

Ile Lys Trp Leu Met Asp Glu Val Glu Cys Arg Val Ile Leu Pro Lys
325 330 335

Phe His Phe Asp Met Thr Asn Glu Leu Lys Glu Ser Leu Val Lys Leu
340 345 350

Gly Ile Ser Gln Ile Phe Thr Ser Glu Ala Ser Leu Pro Ser Leu Ala
355 360 365

Arg Gly Gln Gly Val Gln Asn Arg Leu Gln Val Ser Asn Val Ile Gln
370 375 380

Lys Ala Gly Ile Ile Val Asp Glu Lys Gly Ser Thr Ala Tyr Ala Ala
385 390 395 400

Ser Glu Val Ser Leu Val Asn Lys Phe Gly Asp Asp Glu Phe Val Met
405 410 415

Phe Asn Ala Asn His Pro Phe Leu Phe Thr Ile Glu Asp Glu Thr Thr
420 425 430

Gly Ala Ile Leu Phe Thr Gly Lys Val Val Asp Pro Thr Gln
435 440 445

<210> 50
<211> 1651
<212> DNA
<213> Lutzomyia longipalpis

<220>
<221> misc_feature
<222> (1636)..(1636)
<223> n is a, c, g, or t

<400> 50
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ttaagtgtgt gtgtcttagc aaagtgattt ccacaatgaa gattattttt ttagccgctt 120

ttctactagc ggatggtatt tgggctgctg aagaaccttc agtggaaatt gtaacaccac 180

aatcagtgcg gagacacgct acgccaaaag cccaggacgc gagggtagga agtgaatccg 240

caacaacagc accaagacca agtgaatcaa tggattactg ggagaatgat gatttcgtcc 300

catttgaggg tccattcaag gatattggag aattcgactg gaacctttcg aagatcgttt 360

ttgaggaaaa caaaggtaat gccatcttgt cgccactctc tgtgaagcta ctaatgagtt 420

tgctcttcga ggccagtgcg tcaggtacct tgacccagca ccaactcaga caagccactc 480

ccaccatcgt cacccactat cagtctcgag aattttacaa gaatatcttt gacggtctca 540

agaaaaagag taacgactac acggttcact ttggtacgag aatctacgtg gatcagtttg 600

tgacgcctcg ccagagatat gctgccattt tggagaagca ttatctgact gatctcaaag 660

ttgaggactt ctcgaaggca aaagaaacaa ctcaggcaat caatagttgg gtgtcaaaca 720

tcacaaatga gcacataaag gatctcgtga aggaggaaga tgttcagaat tcagttatgc 780

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ggctctacta cttctacgag gcaaaggaat tggatgctaa gatcctcaga attccttaca 960

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ttgtgcgtca gattaacacg gtcctcctgc acaggattaa gtggttgatg gatgaagtgg 1080

agtgcagggt tattctaccc aagttccact ttgacatgac gaatgagctg aaggaatcgc 1140

tcgtaaagtt gggcatcagt cagattttca catcagaggc atctttgcca tcattagcac 1200

gaggacaggg cgtacagaat cgtctgcagg tgtctaatgt gattcagaag gcgggaataa 1260

ttgtggatga gaagggcagc acagcctatg ctgcgtcaga agtgagccta gtcaacaagt 1320

ttggagatga tgagttcgtc atgttcaacg ctaatcatcc attcctcttt acaattgagg 1380

acgaaaccac cggcgcaatc ctatttacgg gaaaagtcgt cgatcccacg caatagggaa 1440

tgaaaagcat ttcatcgtat acaacttttt ttttaattaa ttattcctca ttgaaggaca 1500

ttaatagagc atcttctcag gaaggcactc ctgacttatt tttactaaat gtgatccttg 1560

gacacataaa aaaaacagct gtactttcta ctttttataa tatacgacca tatttgtgag 1620

gaaaaaaaaa aaaaanaaaa aaaaaaaaaa a 1651

<210> 51
<211> 166
<212> PRT
<213> Lutzomyia longipalpis

<400> 51

Met Arg Phe Leu Leu Leu Ala Phe Ser Val Ala Leu Val Leu Ser Pro
1 5 10 15

Thr Phe Ala Lys Pro Gly Leu Trp Asp Ile Val Thr Gly Ile Asn Asp
20 25 30

Met Val Lys Asn Thr Ala Asn Ala Leu Lys Asn Arg Leu Thr Thr Ser
35 40 45

Val Thr Leu Phe Thr Asn Thr Ile Thr Glu Ala Ile Lys Asn Ala Asn
50 55 60

Ser Ser Val Ser Glu Leu Leu Gln Gln Val Asn Glu Thr Leu Thr Asp
65 70 75 80

Ile Ile Asn Gly Val Gly Gln Val Gln Ser Ala Phe Val Asn Ser Ala
85 90 95

Gly Asn Val Val Val Gln Ile Val Asp Ala Ala Gly Asn Val Leu Glu
100 105 110

Val Val Val Asp Glu Ala Gly Asn Ile Val Glu Val Ala Gly Thr Ala
115 120 125

Leu Glu Thr Ile Ile Pro Leu Pro Gly Val Val Ile Gln Lys Ile Ile
130 135 140

Asp Ala Leu Gln Gly Asn Ala Gly Thr Thr Ser Asp Ser Ala Ser Ser
145 150 155 160

Thr Val Pro Gln Gln Ser
165

<210> 52
<211> 739
<212> DNA
<213> Lutzomyia longipalpis

<400> 52
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aactggtatt aatgatatgg taaaaaatac tgcgaatgca ctcaaaaatc gtctaacaac 180

ttctgtgaca ttattcacaa ataccatcac cgaagctata aaaaatgcaa attcttctgt 240

ttcggaactc cttcagcaag tcaatgaaac ccttacggat attattaatg gtgtaggaca 300

agtgcagagt gcctttgtga attcagctgg aaatgttgtt gtgcaaattg ttgatgccgc 360

tggaaatgtt ttggaagttg ttgttgatga ggctggaaat atcgtggagg tagctggaac 420

agcattggaa actatcattc cactgcccgg tgtagtgatt cagaagataa ttgatgctct 480

ccaaggaaat gcagggacta catcggattc agcttcatca actgtgcccc aacaatctta 540

actacaaccg caatgatgtt gtctttaacg gagaattttt aaatttgaat atcaaaatcc 600

aagatgaaat attcagattt ttcaatcaat atgatacgaa attttgaaat tatttttccg 660

actaaagcaa tttgtaaaag gaaaaccaaa taaatatttg aaattgtaaa gaaaaaaaaa 720

aaaaaaaaaa aaaaaaaaa 739

<210> 53
<211> 109
<212> PRT
<213> Lutzomyia longipalpis

<400> 53

Met Val Lys Tyr Ser Cys Leu Val Leu Val Ala Ile Phe Leu Leu Ala
1 5 10 15

Gly Pro Tyr Gly Val Val Gly Ser Cys Glu Asn Asp Leu Thr Glu Ala
20 25 30

Ala Lys Tyr Leu Gln Asp Glu Cys Asn Ala Gly Glu Ile Ala Asp Glu
35 40 45

Phe Leu Pro Phe Ser Glu Glu Glu Val Gly Glu Ala Leu Ser Asp Lys
50 55 60

Pro Glu Asn Val Gln Glu Val Thr Asn Ile Val Arg Gly Cys Phe Glu
65 70 75 80

Ala Glu Gln Ala Lys Glu His Gly Lys Cys Glu Arg Phe Ser Ala Leu
85 90 95

Ser Gln Cys Tyr Ile Glu Lys Asn Leu Cys Gln Phe Phe
100 105

<210> 54
<211> 447
<212> DNA
<213> Lutzomyia longipalpis

<400> 54
atatcaattt tatcatcatg gtgaagtact cgtgtcttgt tcttgttgca atttttcttc 60

tggccggacc ctacggcgtt gtaggttctt gtgagaatga cctgacagag gccgccaagt 120

atcttcaaga tgaatgcaat gcaggtgaaa ttgcagatga atttctaccc ttctctgaag 180

aagaagtggg tgaagcattg agcgacaaac cagaaaacgt gcaggaagtc accaacatcg 240

tgagaggatg ctttgaagct gaacaagcca aagagcatgg aaaatgtgaa agattttccg 300

ctttgagtca atgctacatt gaaaagaatt tatgtcaatt cttctaaaat attttgaaga 360

aaagttatga atgaaaattt tctgaaattt tgttgcaaaa atatataaat tgcccaatta 420

aaaaaaaaaa aaaaaaaaaa aaaaaaa 447

<210> 55
<211> 115
<212> PRT
<213> Lutzomyia longipalpis

<400> 55

Met Lys Phe Phe Tyr Leu Ile Phe Ser Ala Ile Phe Phe Leu Ala Asp
1 5 10 15

Pro Ala Leu Val Lys Cys Ser Glu Asp Cys Glu Asn Ile Phe His Asp
20 25 30

Asn Ala Tyr Leu Leu Lys Leu Asp Cys Glu Ala Gly Arg Val Asp Pro
35 40 45

Val Glu Tyr Asp Asp Ile Ser Asp Glu Glu Ile Tyr Glu Ile Thr Val
50 55 60

Asp Val Gly Val Ser Ser Glu Asp Gln Glu Lys Val Ala Lys Ile Ile
65 70 75 80

Arg Glu Cys Ile Ala Gln Val Ser Thr Gln Asp Cys Thr Lys Phe Ser
85 90 95

Glu Ile Tyr Asp Cys Tyr Met Lys Lys Lys Ile Cys Asn Tyr Tyr Pro
100 105 110

Glu Asn Met
115

<210> 56
<211> 496
<212> DNA
<213> Lutzomyia longipalpis

<400> 56
agtttaattt tcatcatgaa gttcttctac ttgattttct ctgcaatttt ctttctggct 60

gatcctgctt tggtcaagtg ttcagaggat tgtgagaata ttttttcatga caatgcgtac 120

ctccttaaat tggattgtga agcaggaagg gttgatcctg ttgaatacga cgatatttcg 180

gatgaagaaa tatatgaaat aacggtcgat gttggagttt catctgagga ccaggagaaa 240

gttgcgaaaa taataaggga gtgcattgca caagtttcaa cgcaagattg cacgaaattt 300

tcagaaattt atgattgtta catgaagaag aaaatctgta attattatcc tgaaaatatg 360

taaaaaaaaa ttatttattt atataaaaaa atataaggat taaaatctct tattgattgt 420

aaaaatggcc taatattgaa gcaaaaatta aagcatgaaa caagaccaaa aaaaaaaaaa 480

aaaaaaaaaa aaaaaa 496

<210> 57
<211> 409
<212> PRT
<213> Lutzomyia longipalpis

<400> 57

Met His Leu Gln Leu Asn Leu Cys Ala Ile Leu Leu Ser Val Leu Asn
1 5 10 15

Gly Ile Gln Gly Ala Pro Lys Ser Ile Asn Ser Lys Ser Cys Ala Ile
20 25 30

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Ser Phe Pro Glu Asn Val Thr Ala Lys Lys Glu Pro Val Tyr Leu Lys
        35                  40                  45

Pro Ser Asn Asp Gly Ser Leu Ser Thr Pro Leu Gln Pro Ser Gly Pro
    50                  55                  60

Phe Val Ser Leu Lys Ile Gly Glu Ser Leu Ala Ile Phe Cys Pro Gly
65                  70                  75                  80

Asp Gly Lys Asp Val Glu Thr Ile Thr Cys Asn Thr Asn Phe Asp Leu
                85                  90                  95

Ala Ser Tyr Ser Cys Asn Lys Ser Thr Ser Thr Asp Thr Ile Glu Thr
            100                 105                 110

Glu Glu Val Cys Gly Gly Ser Gly Lys Val Tyr Lys Val Gly Phe Pro
        115                 120                 125

Leu Pro Ser Gly Asn Phe His Ser Ile Tyr Gln Thr Cys Phe Asp Lys
    130                 135                 140

Lys Asn Leu Thr Pro Leu Tyr Ser Ile His Ile Leu Asn Gly Gln Ala
145                 150                 155                 160

Val Gly Tyr His Leu Lys His Thr Arg Gly Ser Phe Arg Thr Asn Gly
                165                 170                 175

            180                 185                 190

Lys Phe Asn Lys Leu Phe Gly Pro Lys Gln Thr Phe Phe Arg Arg Pro
        195                 200                 205

Leu Asn Phe Leu Ser Arg Gly His Leu Ser Pro Glu Val Asp Phe Thr
    210                 215                 220

Phe Arg Arg Glu Gln His Ala Thr Glu Met Tyr Ile Asn Thr Ala Pro
225                 230                 235                 240

Gln Tyr Gln Ser Ile Asn Gln Gly Asn Trp Leu Arg Val Glu Asn His
                245                 250                 255

Val Arg Asp Leu Ala Lys Val Leu Gln Lys Asp Ile Thr Val Val Thr
            260                 265                 270

Gly Ile Leu Gly Ile Leu Arg Leu Lys Ser Lys Lys Ile Glu Lys Glu
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275 280 285

Ile Tyr Leu Gly Asp Asp Val Ile Ala Val Pro Ala Met Phe Trp Lys
290 295 300

Ala Val Phe Asp Pro Gln Lys Gln Glu Ala Ile Val Phe Val Ser Ser
305 310 315 320

Asn Asn Pro His Val Lys Thr Phe Asn Pro Asn Cys Lys Asp Val Cys
325 330 335

Ala Gln Ala Gly Phe Gly Asn Asp Asn Leu Glu Tyr Phe Ser Asn Tyr
340 345 350

Ser Ile Gly Leu Thr Ile Cys Cys Lys Leu Glu Glu Phe Val Lys Arg
355 360 365

Asn Lys Ile Ile Leu Pro Lys Glu Val Asn Asn Lys Asn Tyr Thr Lys
370 375 380

Lys Leu Leu Lys Phe Pro Lys Thr Arg Asn Lys Glu Gly Asp Lys Lys
385 390 395 400

Val Val Arg Lys Arg Ala Lys Gly Ala
405

<210> 58
<211> 1281
<212> DNA
<213> Lutzomyia longipalpis

<400> 58
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gaattcaggg cgctcccaaa agtattaatt caaaatcctg cgcaatctcc tttccggaga 120

atgtaacggc taagaaggag ccagtgtact tgaaaccatc aaatgatggc tcattgagta 180

ccccctaca gccaagtggg ccatttgtaa gtctcaaaat tggagaatct cttgcaatct 240

tctgtccagg tgatggaaag gacgtagaga caattacgtg caatacaaat ttcgatttag 300

cttcatattc gtgcaacaag agcacatcaa cggataccat tgaaacggaa gaagtttgcg 360

gaggaagtgg aaaagtgtac aaagttggtt ttccgctgcc ctctgggaat ttccattcaa 420

tctaccaaac gtgttttgat aagaaaaatc tcacacctct ctactcaatt cacattctca 480

atggtcaagc tgttggatat caccttaagc acacaagagg aagctttcgt accaatggta 540

tctacgggaa agtcaacatt gataaactct acaagacgca aattgagaaa ttcaacaaac 600

ttttcggccc taaacaaaca ttttttccgta gacccctcaa ttttctatca cgtggacact 660

taagccccga agtggacttt acattccgta gggaacaaca tgcaacggaa atgtacatta 720

acacagcacc acagtaccaa tcaattaatc aaggaaattg gctacgtgtt gaaaatcacg 780

tgagggatct cgcaaaagtt ctgcagaagg acataacagt cgttacggga attttgggga 840

tacttcggtt gaagagtaag aaaatagaga aagaaatcta tttaggagat gacgtaattg 900

ccgtaccagc aatgttctgg aaggctgttt ttgaccctca aaaacaagaa gcaattgtct 960

ttgtttcctc aaataatccc cacgtgaaga cctttaatcc caactgcaag gatgtatgcg 1020

ctcaagctgg atttgggaat gataatcttg aatatttctc caattattct attggtctga 1080

ctatttgttg caaacttgag gaatttgtta aaagaaataa aataattcta cccaaagaag 1140

taaataacaa aaactacacc aaaaaactcc ttaagtttcc taaaacaaga aacaaggagg 1200

gagataagaa ggtggtacgt aagcgcgcca aaggagcata aatattaaac gaaaaaaaaa 1260

aaaaaaaaaa aaaaaaaaaa a 1281

<210> 59
<211> 160
<212> PRT
<213> Lutzomyia longipalpis

<400> 59

Met Asn Leu His Leu Ala Ile Ile Leu Phe Val Ser Tyr Phe Thr Leu
1 5 10 15

Ile Thr Ala Thr Asp Leu Ile Glu Lys Glu Leu Ser Asp Cys Lys Lys
20 25 30

Ile Phe Ile Ser Lys Ala Glu Leu Thr Trp Phe Gln Ala Leu Asp Phe
35 40 45

Cys Thr Glu Gln Asn Leu Thr Leu Leu Ser Ile Lys Ser Ala Arg Glu
50 55 60

Asn Asp Glu Val Thr Lys Ala Val Arg Ala Glu Val His Leu Pro Asp
65 70 75 80

Thr Lys Lys Ser His Ile Trp Leu Gly Gly Ile Arg Tyr Asp Gln Asp
85 90 95

Lys Asp Phe Arg Trp Ile Ser Asp Gly Thr Thr Val Thr Lys Thr Val
100 105 110

Tyr Ile Asn Trp Tyr Gln Gly Glu Pro Asn Gly Gly Arg Tyr Gln Lys

115 120 125

Glu Phe Cys Met Glu Leu Tyr Phe Lys Thr Pro Ala Gly Gln Trp Asn
130 135 140

Asp Asp Ile Cys Thr Ala Lys His His Phe Ile Cys Gln Glu Lys Lys
145 150 155 160

<210> 60
<211> 671
<212> DNA
<213> Lutzomyia longipalpis

<400> 60
gttctacgat aaaattttct tttcaaactt ttcttttaaa gaaaaatctt caaaaagtta 60

aaatgaattt gcaccttgcg attatcctct ttgtgagtta cttcacactg atcactgcta 120

cggatctaat tgaaaaggaa ctttctgatt gcaaaaagat cttcatctcc aaggctgagc 180

taacttggtt ccaagctctc gatttctgta ccgaacaaaa cctaactttg ctctcaatta 240

aatccgcccg ggaaaatgat gaggtgacta aagcagttcg agctgaggtt catcttccag 300

acacaaagaa gtctcacatt tggctcggag gtattcgtta tgatcaagac aaggatttcc 360

gttggataag cgatggaaca actgttacga agacagtcta catcaattgg taccaaggag 420

aaccaaatgg tgggaggtac caaaaggaat tttgtatgga attgtacttt aaaactccag 480

ctggtcaatg gaatgatgat atttgtacag caaagcatca ttttatatgt caggagaaaa 540

aataaattga attgttcatg tgtctttggc ggtgcgaagg tataattcag gttgacgaca 600

taaattgatt tttctttcat taagaaaata aaggcttgaa tttataaaaa aaaaaaaaaa 660

aaaaaaaaaa a 671

<210> 61
<211> 160
<212> PRT
<213> Lutzomyia longipalpis

<400> 61

Met Asn Leu Pro Leu Ala Ile Ile Leu Phe Val Ser Tyr Phe Thr Leu
1 5 10 15

Ile Thr Ala Ala Asp Leu Thr Glu Lys Glu Leu Ser Asp Gly Lys Lys
20 25 30

Ile Phe Ile Ser Lys Ala Glu Leu Ser Trp Phe Asp Ala Leu Asp Ala
35 40 45

Cys Thr Glu Lys Asp Leu Thr Leu Leu Thr Ile Lys Ser Ala Arg Glu
50 55 60

Asn Glu Glu Val Thr Lys Ala Val Arg Ala Glu Val His Leu Pro Asp
65 70 75 80

Thr Lys Lys Ser His Ile Trp Leu Gly Gly Ile Arg Tyr Asp Gln Asp
85 90 95

Lys Asp Phe Arg Trp Ile Ser Asp Gly Thr Thr Val Thr Lys Thr Val
100 105 110

Tyr Ile Asn Trp Tyr Gln Gly Glu Pro Asn Gly Gly Arg Tyr Gln Lys
115 120 125

Glu Phe Cys Met Glu Leu Tyr Phe Lys Thr Pro Ala Gly Gln Trp Asn
130 135 140

Asp Asp Ile Cys Thr Ala Lys His His Phe Ile Cys Gln Glu Lys Lys
145 150 155 160

<210> 62
<211> 672
<212> DNA
<213> Lutzomyia longipalpis

<400> 62
gttctacgat aaaattttct tttcaaactt ttcttttaaa gaaaaatctt caaaaagtta 60

aaatgaattt gccccttgcg attatcctct ttgtgagtta cttcacactg atcactgctg 120

cggatctaac tgaaaaggaa ctttctgatg gcaaaaagat cttcatctcc aaggctgagc 180

taagttggtt cgatgctctc gatgcctgta ccgaaaaaga cctaactttg ctcacaatta 240

aatccgcccg ggaaaatgag gaagtgacta aagcagttcg agctgaggtt catcttccag 300

acacaaagaa gtctcacatt tggctcggag gtattcgtta tgatcaagac aaggatttcc 360

gttggataag cgatggaaca actgttacga agacagtcta catcaattgg taccaaggag 420

aaccaaatgg tgggaggtac caaaaggaat tttgtatgga attgtacttt aaaactccag 480

ctggtcaatg gaatgatgat atttgtacag caaagcatca ttttatatgt caggagaaaa 540

aataaattga attgttcatg tgtctttggc ggtgcgaagg tataattcag gttgacgaca 600

taaattgatt tttctttcat taagaaaata aaggcttgaa tttagcaaaa aaaaaaaaaa 660

aaaaaaaaaa aa 672

<210> 63
<211> 399

<212> PRT
<213> Lutzomyia longipalpis

<400> 63

Met Lys Val Phe Phe Ser Ile Phe Thr Leu Val Leu Phe Gln Gly Thr
1 5 10 15

Leu Gly Ala Asp Thr Gln Gly Tyr Lys Trp Lys Gln Leu Leu Tyr Asn
20 25 30

Asn Val Thr Pro Gly Ser Tyr Asn Pro Asp Asn Met Ile Ser Thr Ala
35 40 45

Phe Ala Tyr Asp Ala Glu Gly Glu Lys Leu Phe Leu Ala Val Pro Arg
50 55 60

Lys Leu Pro Arg Val Pro Tyr Thr Leu Ala Glu Val Asp Thr Lys Asn
65 70 75 80

Ser Leu Gly Val Lys Gly Lys His Ser Pro Leu Leu Asn Lys Phe Ser
85 90 95

Gly His Lys Thr Gly Lys Glu Leu Thr Ser Ile Tyr Gln Pro Val Ile
100 105 110

Asp Asp Cys Arg Arg Leu Trp Val Val Asp Ile Gly Ser Val Glu Tyr
115 120 125

Arg Ser Arg Gly Ala Lys Asp Tyr Pro Ser His Arg Pro Ala Ile Val
130 135 140

Ala Tyr Asp Leu Lys Gln Pro Asn Tyr Pro Glu Val Val Arg Tyr Tyr
145 150 155 160

Phe Pro Thr Arg Leu Val Glu Lys Pro Thr Tyr Phe Gly Gly Phe Ala
165 170 175

Val Asp Val Ala Asn Pro Lys Gly Asp Cys Ser Glu Thr Phe Val Tyr
180 185 190

Ile Thr Asn Phe Leu Arg Gly Ala Leu Phe Ile Tyr Asp His Lys Lys
195 200 205

Gln Asp Ser Trp Asn Val Thr His Pro Thr Phe Lys Ala Glu Arg Pro
210 215 220

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Thr Lys Phe Asp Tyr Gly Gly Lys Glu Tyr Glu Phe Lys Ala Gly Ile
225                 230                 235                 240

Phe Gly Ile Thr Leu Gly Asp Arg Asp Ser Glu Gly Asn Arg Pro Ala
                245                 250                 255

Tyr Tyr Leu Ala Gly Ser Ala Ile Lys Val Tyr Ser Val Asn Thr Lys
            260                 265                 270

Glu Leu Lys Gln Lys Gly Gly Lys Leu Asn Pro Glu Leu Leu Gly Asn
        275                 280                 285

Arg Gly Lys Tyr Asn Asp Ala Ile Ala Leu Ala Tyr Asp Pro Lys Thr
    290                 295                 300

Lys Val Ile Phe Phe Ala Glu Ala Asn Thr Lys Gln Val Ser Cys Trp
305                 310                 315                 320

Asn Thr Gln Lys Met Pro Leu Arg Met Lys Asn Thr Asp Val Val Tyr
                325                 330                 335

Thr Ser Ser Arg Phe Val Phe Gly Thr Asp Ile Ser Val Asp Ser Lys
            340                 345                 350

Gly Gly Leu Trp Phe Met Ser Asn Gly Phe Pro Pro Ile Arg Lys Ser
        355                 360                 365

Glu Lys Phe Lys Tyr Asp Phe Pro Arg Tyr Arg Leu Met Arg Ile Met
    370                 375                 380

Asp Thr Gln Glu Ala Ile Ala Gly Thr Ala Cys Asp Met Asn Ala
385                 390                 395
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<210> 64
<211> 1429
<212> DNA
<213> Lutzomyia longipalpis

<400> 64

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agggaccctt ggagcggata ctcaaggata taaatggaag caattgctct acaataatgt    120

tacaccagga tcctacaatc cggataatat gatcagtacg gcttttgcct acgatgctga    180

gggtgaaaaa ctcttcctag ctgtcccaag gaagttaccc agagttccgt atacattggc    240

ggaagtggat acaaagaata gtcttggtgt taagggaaaa cattcaccgt tacttaacaa    300

attcagtggg cacaaaactg ggaaggaact aacatcaatc tatcagccag ttattgatga    360
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ttgtcgtcgc ctttgggtgg ttgatattgg ttccgtggaa tatcgctcaa gaggtgccaa 420

agactacccg agtcatcgtc ctgcaattgt tgcgtacgac ctaaagcaac caaactaccc 480

cgaagttgtt cgatactatt tccccacaag attagtggag aagccaacat atttcggtgg 540

atttgccgtt gatgttgcaa acccaaaggg ggattgtagt gaaacttttg tctacattac 600

aaacttcctc aggggagctc tctttatata cgatcataag aagcaggatt cgtggaatgt 660

aactcatccc accttcaaag cagaacgacc cactaaattt gattacggcg gaaaggaata 720

tgaattcaaa gccggaattt tcggaattac tctcggagat cgagacagtg aaggcaatcg 780

tccagcttac tacttagccg gaagtgccat caaagtctac agcgtcaaca cgaaagaact 840

taagcagaag ggtggaaagc tgaatccgga gcttcttgga aaccgcggga agtacaacga 900

tgccattgcc ctagcttacg atcccaaaac taaagttatc ttctttgctg aggccaacac 960

aaagcaagta tcctgctgga acacacagaa aatgccactg aggatgaaga ataccgacgt 1020

agtctacact agttctcgct ttgtctttgg aacggacatt tcggttgata gcaagggcgg 1080

cctctggttc atgtctaacg gctttccgcc tataaggaaa tcagaaaaat tcaaatatga 1140

cttcccacgc taccgtctaa tgaggatcat ggacacacag gaagcaattg ccggaactgc 1200

ttgcgatatg aatgcataaa agttaatttt caacccaaga agaagaccta aagaggcttt 1260

tccaggcttt gatgcaggag aggtggttat caacgcaaaa tcagctattg ttgtatgagg 1320

aggagaaatt attgattctg aattctataa aaaaaattta atttgtgaaa tatttggcaa 1380

taataaatta attgaattac aaaaaaaaaa aaaaaaaaaa aaaaaaaaa 1429

<210> 65
<211> 170
<212> PRT
<213> Lutzomyia longipalpis

<400> 65

Met Gln Ser Lys Ile Leu Ser Phe Val Leu Phe Thr Leu Ser Leu Gly
1 5 10 15

Tyr Val Leu Gly Glu Thr Cys Ser Asn Ala Lys Val Lys Gly Ala Thr
20 25 30

Ser Tyr Ser Thr Thr Asp Ala Thr Ile Val Ser Gln Ile Ala Phe Val
35 40 45

Thr Glu Phe Ser Leu Glu Cys Ser Asn Pro Gly Ser Glu Lys Ile Ser
50 55 60

```
Leu Phe Ala Glu Val Asp Gly Lys Ile Thr Pro Val Ala Met Ile Gly
65                  70                  75                  80

Asp Thr Thr Tyr Gln Val Ser Trp Asn Glu Glu Val Asn Lys Ala Arg
                85                  90                  95

Ser Gly Asp Tyr Ser Val Lys Leu Tyr Asp Glu Glu Gly Tyr Gly Ala
            100                 105                 110

Val Arg Lys Ala Gln Arg Ser Gly Glu Glu Asn Lys Val Lys Pro Leu
        115                 120                 125

Ala Thr Val Val Val Arg His Pro Gly Thr Tyr Thr Gly Pro Trp Phe
    130                 135                 140

Asn Ser Glu Ile Leu Ala Ala Gly Leu Ile Ala Val Val Ala Tyr Phe
145                 150                 155                 160

Ala Phe Ser Thr Arg Ser Lys Ile Leu Ser
                165                 170
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<210> 66
<211> 712
<212> DNA
<213> Lutzomyia longipalpis

<400> 66

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atgcagtcaa aaattctttc tttcgtcctt ttcaccttat ccttgggcta tgttttgggt    120

gaaacatgct caaatgctaa ggttaaggga gctacctctt attccacaac ggatgccaca    180

attgtaagcc aaattgcctt tgtgactgaa ttctccttgg aatgctcaaa tcctggatcc    240

gagaaaatct ccctatttgc tgaagtcgat ggcaaaatta ctcctgttgc catgatcggg    300

gataccacct accaggtgag ctggaatgaa gaggttaata aggctagaag tggtgactac    360

agtgtgaagc tgtacgatga agaaggatac ggagcagtac gcaaagctca gagatcaggt    420

gaagagaaca aggtcaaacc actagcaacc gttgttgttc gacatccagg aacatacact    480

ggaccatggt tcaattccga aatcctcgca gctggtctca ttgctgttgt tgcctacttt    540

gctttctcaa cgcgaagcaa aattctttcc taaagagacg cagcatgaaa tttcacaaaa    600

aaataaaaac aaattcaagt catcaaccat gtctctttgg cactcagact gtttctgtga    660

aatacaaact attatttaac aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aa            712
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<210> 67
<211> 73

<212> PRT
<213> Lutzomyia longipalpis

<400> 67

Met Val Ser Ile Leu Leu Ile Ser Leu Ile Leu Asn Leu Leu Val Phe
1 5 10 15

Tyr Ala Lys Ala Arg Pro Leu Glu Asp Ile Ser Ser Asp Leu Ser Pro
20 25 30

Asp Tyr Tyr Ile Thr Glu Gly Tyr Asp Gly Val Lys Glu Lys Arg Glu
35 40 45

Ile Glu Leu Val Pro Val Thr Phe Gly Ile Phe Asn Ile His Thr Thr
50 55 60

Pro Ala Pro Arg Ile Thr Phe Glu Trp
65 70

<210> 68
<211> 379
<212> DNA
<213> Lutzomyia longipalpis

<400> 68
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gttggttttc tatgctaaag ctagaccact agaagacatc tcgtcagatc tttcccctga 120

ttattacatc actgaaggct atgacggtgt gaaggagaag agagagatcg aacttgtacc 180

tgtgacattt ggaatattta atatacatac aacacctgct cccagaatta cctttgaatg 240

gtaaaaaatc caagaagaat ttatgatttt attcttcctt ccattgggat ggattgtaag 300

tcagcataaa acgccgttaa aaatgaattt ttaataaaaa aaaattattc caaaaaaaaa 360

aaaaaaaaaa aaaaaaaaa 379

<210> 69
<211> 76
<212> PRT
<213> Lutzomyia longipalpis

<400> 69

Met Lys Leu Phe Cys Leu Ile Phe Val Val Phe Val Ala Leu Glu Val
1 5 10 15

Cys Ile Glu Thr Val Lys Ala Met Glu Ala Thr Glu Glu Ile Ser Val
20 25 30

Lys Leu Gln Asp Asp Ala Asn Glu Pro Asp Asp Ser Leu Asp Leu Asp
35 40 45

Glu Gly Leu Pro Asp Ala Phe Asp Glu Asp Tyr Asn Asn Gln Ala Glu
50 55 60

Tyr Lys Pro Asn Pro Arg Gly Asp Tyr Arg Arg Arg
65 70 75

<210> 70
<211> 526
<212> DNA
<213> Lutzomyia longipalpis

<400> 70
cactattcat tggaagattt attaacttca agatgaaatt attttgttta atttttgttg 60

tgtttgttgc tttagaagtc tgtatagaga ccgtgaaagc tatggaagca acggaggaga 120

tatctgtaaa attgcaagat gatgcgaatg aacctgatga ctctctggat ttagacgaag 180

gtcttcctga tgcattcgat gaggactata ataatcaggc tgagtacaag ccgaatccta 240

gaggggacta cagaagacga taattaatat aaattcagga aaacactcta aaaatttcca 300

attgactcta ctttaaacga tttaatacct acctacacta aataccatat gcaataatta 360

tgttttaatt atttagtgca agatctacta gtttcagttc atattttggg actttcccgc 420

ctttctctcg atggaaaaat gattttacgg attcttaatt ttcattgtac agagttaata 480

aaacaattga aagcaattaa aaaaaaaaaa aaaaaaaaaa aaaaaa 526

<210> 71
<211> 22
<212> DNA
<213> Artificial sequence

<220>
<223> Oligonucleotide primer

<400> 71
aagtactcta gcaattgtga gc 22

<210> 72
<211> 22
<212> DNA
<213> Artificial sequence

<220>
<223> Oligonucleotide primer

<400> 72
ctcttcgcta ttacgccagc tg 22

<210> 73
<211> 24
<212> DNA
<213> Artificial sequence

<220>
<223> Oligonucleotide primer

<400> 73
tctcgggaag cgcgccattg tgtt 24